アイセントレス錠600mg
に関する資料

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

1 BACKGROUND AND OVERVIEW

Raltegravir (also known as ISENTRESS®, MK-0518, and L-000900612) is a human immunodeficiency virus (HIV)-1 integrase strand transfer inhibitor with potent in vitro activity against HIV-1, exhibiting a 95% inhibitory concentration (IC_{95}) of 33 nM in the presence of 50% human serum. It is available and marketed as a 400 mg film-coated tablet formulation containing poloxamer in patients weighing at least 25 kg, as a chewable tablet formulation in 100 mg (scored) and 25 mg strengths for patients weighing at least 10 kg, and as granules for suspension in patients weighing at least 3 kg. Raltegravir for once daily (QD) use, at a dose of 1200 mg (2 x 600 mg tablets), offers a new treatment option for the initial treatment of HIV-1 infected subjects and has exhibited an excellent safety, tolerability, and efficacy profile as described within this Application (referred to as the Once Daily Application).

Two tablet strengths of different formulation compositions were considered for the feasibility of once-daily dosing. One tablet strength was the existing marketed 400 mg tablet and the second a newly-formulated 600 mg tablet. Data from the Phase 1 studies PN290 and PN291, which provided the relevant biopharmaceutic and pharmacokinetic characterization of the 1200 mg dose using the two tablet strengths in fasted and fed states, and PN293, which provided safety and pharmacokinetic experience at a dose higher than 1200 mg, together with modeling and simulation, resulted in selection of the 600 mg tablet strength (1200 mg dose as 2 x 600 mg tablets) for further evaluation as once daily dosing in the Phase 3 study PN292. The raltegravir 600 mg tablet for once daily use is a non-poloxamer based film-coated dosage form, differing from the 400 mg tablet by higher drug loading and better processability.

Three 600 mg tablet formulations were used in the raltegravir Once Daily Development Program (see [Table 2.7.1: 1]: 1) Phase 1 tablet (used in PN290, PN291 and PN293), 2) Phase 3 tablet (used in PN292), and 3) final market image (FMI) tablet (used in the drug-drug interaction [DDI] studies PN812, PN823, and PN824). The Phase 1 and Phase 3 tablets differed only in minor change to the non-functional film-coat composition (addition of colorant). The tablets used in Phase 3 and the FMI tablet used in the DDI studies had different OPADRY® non-functional film-coating compositions and were demonstrated to be similar in comparative dissolution studies.

The biopharmaceutics of raltegravir 1200 mg QD were assessed in two Phase 1 studies (PN290 and PN291) conducted in healthy subjects. The results of these studies, together with modeling and simulation, confirmed that 1200 mg QD (administered as 2 x 600mg tablets) had a pharmacokinetic profile likely to result in efficacy that would be non-inferior to 400 mg BID, and were instrumental in selecting the raltegravir 600 mg tablet for further clinical development. In PN290, the effect of food on the pharmacokinetics of the 1200 mg dose using the 600 mg tablet strength under both high-fat and low-fat conditions were similar to or smaller than those observed with the 400 mg BID formulation. A viral dynamics PK/PD model developed using PK and efficacy data from prior raltegravir clinical studies and linking antiviral efficacy to the raltegravir PK profile was used to assess the probability of demonstrating the non-inferiority of raltegravir 1200 mg QD compared to 400 mg BID. Simulations from the viral dynamics model using PK data from PN290 and PN291 predicted

that raltegravir formulated for once daily use, at a dose of 1200 mg QD (2 x 600 mg tablets) will have efficacy similar to raltegravir 400 mg BID.

The effect of food on a single dose of raltegravir 1200 mg QD (2 x 600 mg tablets) was assessed in PN290. Administration of a low fat meal decreased the rate and extent of absorption of raltegravir 1200 mg QD (2 x 600 mg tablets); on average there was a 42% decrease in $AUC_{0\text{-last}}$, 52% decrease in C_{max}, and 16% decrease in C_{24hr} compared to the fasted state. Administration of a high fat meal decreased the rate but not the extent of absorption of raltegravir 1200 mg QD (2 x 600 mg tablets) (on average, a 1.9% increase in $AUC_{0\text{-last}}$, 28% decrease in C_{max}, and 12% decrease in C_{24hr}). The decrease in raltegravir exposure using 2 x 600 mg tablets observed following a low fat meal is consistent with the food effect observed for the 400 mg BID formulation, while the changes observed following a high fat meal were less than those observed for the 400 mg BID formulation ([Ref. 5.3.1.1: P290]). Simulations were used to explore the impact of the food effect observed in PN290 and indicated that efficacy was likely to be maintained even in a scenario where raltegravir is taken consistently with a low-fat meal. Consequently, the 600 mg tablet formulated for once daily use was carried forward into the Phase 3 study PN292, with instructions to administer without regard to food intake.

The raltegravir 600 mg tablet for once-daily use is a non-poloxamer based film-coated dosage form, different from the marketed 400 mg film-coated tablet containing poloxamer by higher drug loading and better processability. Additionally, the 600 mg tablet had similar or smaller food effects when studied under high-fat and low-fat meal conditions when compared to the 400 mg tablet. The updated raltegravir product labeling, which is submitted with this Application, instructs that the 400 mg tablet is not intended for QD use and the 600 mg tablet is not intended for BID use, and are therefore, not interchangeable. Subjects should not switch between the 400 mg (for BID) and 600 mg (for QD) tablet of raltegravir without first consulting with their physician or healthcare provider. In addition, the safety and efficacy results from the 1200 mg QD (2 x 600 mg tablets) arm of PN292 support the appropriateness of this dose and formulation for once daily dosing, and that the food effect observed in PN290 is not of clinical importance. Therefore, raltegravir 1200 mg QD can be dosed without regard to food as indicated in the updated raltegravir product labeling.

1.1 Raltegravir Once Daily Formulation Development

This section briefly summarizes the physicochemical properties of raltegravir and the formulation development of the raltegravir 600 mg tablet. Additional information concerning formulation development can be found in [Sec. 2.3.P.2].

Physicochemical Properties

The drug substance (raltegravir) used in the 600 mg tablet is manufactured using the same synthetic process as that utilized for the currently marketed 400 mg tablet and meets the same quality attributes except that the drug substance is milled for use in the 600 mg tablet.

Formulation Development

A 600 mg film-coated tablet formulation has been developed and is proposed for commercialization. The description of the final market image (FMI) 600 mg tablet is provided in [Sec. 2.3.P.5]. The details on formulation development are provided in [Sec. 2.3.P.2]. A listing of the formulations of the 600 mg tablet used in each clinical study in the Once Daily Development Program and a summary of the formulations of the 600 mg tablet are provided in [Table 2.7.1: 1] and [Table 2.7.1: 2], respectively.

Phase 1 to Phase 3 Tablet Formulation:

A white OPADRY® film-coat was used for the tablet evaluated in the Phase 1 studies PN290, PN291 and PN293 (Phase 1 Tablet), while the tablet evaluated in the Phase 3 PN292 study (Phase 3 Tablet) was coated with the same film-coat with colorants. This is regarded as a minor formulation change. The cores of the Phase 1 and Phase 3 tablets are identical in composition.

Phase 3 to FMI Tablet Formulation:

As shown in [Table 2.7.1: 2], the differences between the Phase 3 tablet and the FMI tablet consist of: (1) different OPADRY® non-functional film-coatings, (2) addition of [redacted], and (3) [redacted]. The cores of the Phase 3 and FMI tablets are identical in composition. The Phase 3 and FMI tablets were evaluated by performing in vitro comparative dissolution studies in accordance with appropriate regulatory guidelines. The dissolution profiles are presented in [Sec. 2.3.P.2] and demonstrate similarity between the two formulations.

Table 2.7.1: 1

Formulations Used in the Development Program of the Raltegravir 600 mg Tablet

Protocol Number	Protocol Description	Tablet Formulation
290	A Phase 1 Single Dose Food Effect Study of Raltegravir Formulations	Phase 1
291	A Phase 1 Multiple Dose Study of Raltegravir Formulations	Phase 1
292	A Phase 3 Multicenter, Double-Blind, Randomized, Active Comparator-Controlled Clinical Trial to Evaluate the Safety and Efficacy of Reformulated Raltegravir 1200 mg Once Daily Versus Raltegravir 400 mg Twice Daily, Each in Combination With TRUVADA™, in Treatment-Naïve HIV-1 Infected Subjects	Phase 3
293	A Phase 1 Multiple Dose, Randomized, Double-blind, Placebo-controlled, 2-Treatment Study to Evaluate the Safety and Tolerability and to Assess the Pharmacokinetics of MK-0518 in Healthy Adult Subjects	Phase 1
812	A Phase 1 Study to Evaluate the Influence of Efavirenz on a Single Dose of MK-0518 in Healthy Subjects	FMI
823	A Phase 1 Study to Evaluate the Influence of Atazanavir on a Single Dose of MK-0518 in Healthy Subjects	FMI
824	A Phase 1 Study to Evaluate the Influence of Metal Cation-Containing Antacids on MK-0518 Pharmacokinetics in HIV-Infected Subjects on a Stable Raltegravir-Containing Regimen	FMI

Data Source: [Sec. 3.2.P.2.2]

Table 2.7.1: 2

Summary of Formulations Used in the Development Program of the Raltegravir 600 mg Tablet

Components	Function	Phase 1 Tablet mg/tablet	Phase 3 Tablet mg/tablet	FMI Tablet mg/tablet
MK-0518 (raltegravir) granulation				
Raltegravir Potassium Salt (Raltegravir, MK-0518)*	Active	651.6 (600)	651.6 (600)	651.6 (600)
Hypromellose	Binder	[redacted]	[redacted]	[redacted]
Croscarmellose Sodium	Disintegrant	[redacted]	[redacted]	[redacted]
Water, purified‡	Solvent	[redacted]	[redacted]	[redacted]
[redacted]		[redacted]	[redacted]	[redacted]
[redacted]				
Microcrystalline Cellulose	Filler	[redacted]	[redacted]	[redacted]
Croscarmellose sodium	Disintegrant	[redacted]	[redacted]	[redacted]
Magnesium Stearate	Lubricant	[redacted]	[redacted]	[redacted]
Core tablet Weight (mg)		[redacted]	[redacted]	[redacted]
Film Coating Suspension				
Film Coat, OPADRY®II [redacted]	Film coating agent	[redacted]	-	-
Film Coat, OPADRY®II [redacted]	Film coating agent	-	[redacted]	-
Film Coat, Yellow OPADRY®II [redacted]	Film coating agent	-	-	[redacted]
Water, purified‡	Solvent	[redacted]	[redacted]	[redacted]
Wax				
Carnauba Wax	Wax	[redacted]	[redacted]	[redacted]
Coated Tablet Weight (mg)		[redacted]	[redacted]	[redacted]

* Raltegravir/MK-0518 is delivered as the potassium salt. Conversion factor: 1.086 g of the salt = 1.0 g of the neutral form.
‡ Removed during processing.

Data Source: [Sec. 3.2.P.2.2]

1.2 Raltegravir Once Daily Formulation - In Vitro Dissolution

The dissolution method for the raltegravir 600 mg tablet is provided in [Sec. 2.3.P.5].

The dissolution profile of raltegravir in the 600 mg tablet is consistent with an immediate release dosage form; there was no deliberate effort in the formulation or manufacturing process development to modify the release rate of the drug substance from the drug product dosage form. In [Figure 2.7.1: 1], the dissolution profiles of raltegravir in the 400 mg tablet and raltegravir in the 600 mg tablet in [redacted] ([redacted]) are presented. The in vitro dissolution profile of raltegravir in the 600 mg tablet showed a difference from the reference formulation (400 mg tablet), and Phase 1 studies (PN290 and PN291) were conducted to assess whether this difference in dissolution profiles had a clinically significant effect on the pharmacokinetics of raltegravir (see [Sec. 2.7.1.2.1]).

Figure 2.7.1: 1

Dissolution Profiles of the Raltegravir 400 mg and 600 mg Tablets

Data Source: [Sec. 3.3], [Ref. 5.4: 04DLSJ]

1.3 Raltegravir Once Daily Formulation In Vivo Performance

The pharmacokinetic characteristics of the 400 mg tablet and the 600 mg Phase 1 tablet formulation were compared in two clinical studies, PN290 and PN291. For a description of the study design and results, refer to [Sec. 2.7.1.2.1]. Based on the results of PN290 and PN291, a tablet strength of 600 mg was selected for further clinical development.

Additional pharmacokinetic and modeling data from the other Phase 1 clinical studies are summarized in [Sec. 2.7.2], which focuses on the clinical pharmacology aspects of the development program.

1.4 Bioanalytical Methods

Concentrations of raltegravir in human plasma were determined using a liquid chromatography-tandem mass spectrometric detection (LC-MS/MS) method that was validated in accordance with current regulatory guidance (FDA Guidance for Industry: Bioanalytical Method Validation (2001) [Ref. 5.4: 03QWGP]; EMEA Guideline on Bioanalytical Method Validation (2011) [Ref. 5.4: 03TSXC]).

The development and validation of the bioanalytical method as well as the analyses of raltegravir in clinical samples reported in this Application were performed by [redacted] in [redacted] Netherlands [redacted]

Complete details on the analytical method, assay validation, and sample stability for raltegravir can be found in the study bioanalytical reports that are included as appendices to the clinical study reports: PN290 [Ref. 5.3.1.1: P290], PN291 [Ref. 5.3.1.1: P291], PN292 [Ref. 5.3.5.1: P292V01], PN293 [Ref. 5.3.3.1: P293], PN812 [Ref. 5.3.2.2: P812], PN823 [Ref. 5.3.2.2: P823], PN824 [Ref. 5.3.2.2: P824]. A brief overview of bioanalytical method DM-712A (also known as [redacted]) which was used to support all the bioanalytical analyses, together with a list of the analytical figures of merit to demonstrate assay performance, is presented below and in [Table 2.7.1: 3], respectively.

Sample Collection at the Clinical Sites

Plasma samples for the raltegravir assay were collected using potassium EDTA as anti-coagulant and the aliquots were stored at -20ºC until assayed. Individual collection procedures for specific studies are contained in the clinical protocols. Samples were shipped from clinical sites to the analysis laboratory frozen on dry ice.

Assay Procedures and Conditions

Raltegravir and its internal standard, $^{13}C_6$-raltegravir, were isolated from 200 µL of human plasma using heptane:methylene chloride liquid-liquid extraction followed by liquid chromatography separation. A tandem mass spectrometer with a turbo ion-spray (TISP) interface in the positive ionization mode was used to detect raltegravir and internal standard via multiple reaction monitoring (MRM) in their characteristic precursor → product ion channels at *m/z* 448 → 361 and 451 → 367, respectively. The raltegravir calibration curve range was 2 to 1000 ng/mL.

Table 2.7.1: 3

Analytical Figures of Merit for Raltegravir Plasma Assay (DM-712A/150740MWP0518HPL_S_V3)

	n	Mean (%)
Intra-day Accuracy with Quality Control Samples [1]	5	100.0 – 103.3
Intra-day Precision (CV) with Quality Control Samples [1]	5	0.4 – 3.2
Inter-day Accuracy with Calibration Standards [2]	10	93.3 – 104.6
Inter-day Precision (CV) with Calibration Standards [2]	10	2.1 – 5.5
Inter-day Accuracy with Quality Control Samples [2]	18-19	97.0 – 100.7
Inter-day Precision (CV) with Quality Control Samples [2]	18-19	3.5 – 5.6
Extraction Recovery of Analyte	3	74 – 75
IS Normalized Matrix Factor	8	0.98
Accuracy of Dilution Integrity (5X, 10X, 20X, 50X; up to 40,000 ng/mL)	5	99.0 – 103.2
Precision (CV) of Dilution Integrity	5	0.9 – 2.1
Accuracy of Reinjection Reproducibility Quality Control Samples at 4ºC for 25 hours	5	93.3 – 100.8
Precision (CV) of Reinjection Reproducibility Quality Control Samples at 4ºC for 25 hours	5	0.5 – 3.6
Post-Preparative Extract Stability Accuracy (stored at -20ºC for 26 days)	5	101.3 – 103.3
Post-Preparative Extract Stability Precision (CV) (stored at -20ºC for 26 days)	5	1.5 – 4.8
Accuracy of Quality Control Samples after 5 Freeze/Thaw Cycles (-20ºC)	5	86.4 – 95.0
Precision (CV) of Quality Control Samples after 5 Freeze/Thaw Cycles (-20ºC)	5	8.5 – 14.2
Accuracy of Quality Control Samples after Room Temperature Storage for 13 Hours	5	94.8 – 99.8
Precision (CV) of Quality Control Samples after Room Temperature Storage for 13 Hours	5	1.0 – 3.3
Accuracy of Long-Term Storage Stability (343 Days): -20ºC	5	87.2 – 98.0
Accuracy of Long-Term Storage Stability (23 Days): -70ºC	5	104.4 – 108.9
Incurred Sample Re-analysis (% Within Specification) [2]	40	100

[1] Representative data from validation core run 2 (Watson run 5)
[2] Representative data from Study (P823) (Approximately 378 human plasma samples analyzed in 5 runs)

Data Source: DM-712A Validation Report appended to [Ref. 5.3.2.2: P823]

2 SUMMARY OF RESULTS OF INDIVIDUAL STUDIES

2.1 Summary of Biopharmaceutic Studies

This section provides a brief summary of the two biopharmaceutic studies (PN290 and PN291) that were conducted as part of the development program. The studies were conducted to evaluate the biopharmaceutics of the marketed raltegravir 400 mg tablet and the investigational 600 mg tablet in healthy subjects and included a single dose food effect study

(PN290) and a multiple dose pharmacokinetic study (PN291). A tabular summary of the PK and safety results from each study is provided in [Appendix 2.7.1: 1]. A narrative summary of the PK from each study is provided below.

2.1.1 Single Dose Food Effect Study (PN290)

This study was an open-label, single-dose, randomized, three-period, three-treatment, six-sequence, crossover, food-effect assessment performed in two cohorts in 36 healthy, adult male and female subjects. The pharmacokinetic profile of both the 600 mg (Cohort 1: 18 subjects) and 400 mg (Cohort 2: 18 subjects) tablets under fed (low-fat and high-fat) and fasted conditions at a 1200 mg dose (either as 3 x 400 mg tablets or 2 x 600 mg tablets) were characterized. There was at least a 4-day washout in between treatment periods. Blood samples were collected for 48 hours following each single dose administration of study drug.

Administration of a 1200 mg dose as 2 x 600 mg tablets in the fasted state resulted in a geometric mean (GM) (between-subject coefficient of variation [CV%]) C_{24hr} of 57.7 nM (44%), C_{max} of 22.6 µM (43%), and $AUC_{0\text{-}last}$ of 56.5 µM-hr (38%). Administration of a low-fat meal resulted in a 42% decrease in $AUC_{0\text{-}last}$, 52% decrease in C_{max}, and 16% decrease in C_{24hr}. Administration of a high-fat meal resulted in a 1.9% increase in $AUC_{0\text{-}last}$, 28% decrease in C_{max}, and 12% decrease in C_{24hr}.

Administration of a 1200 mg dose as 3 x 400 mg tablets in the fasted state resulted in a GM (CV%) C_{24hr} of 46.7 nM (31%), C_{max} of 9.2 µM (87%), and $AUC_{0\text{-}last}$ of 33.8 µM-hr (66%). Administration of a low-fat meal resulted in a 73% decrease in $AUC_{0\text{-}last}$, 75% decrease in C_{max}, and 18% decrease in C_{24hr}. Administration of a high-fat meal resulted in a 39% increase in $AUC_{0\text{-}last}$, 23% decrease in C_{max}, and 70% increase in C_{24hr}.

Food caused alterations in raltegravir exposure. In order to assess the clinical significance of these changes in exposure with food for the different formulations, a modeling and simulation based approach was used. Refer to [Sec. 2.7.1.3.2] for the integrated analysis for the assessment of food effect which demonstrates using modeling and simulation methodology that food does not cause clinically significant changes in exposure.

A summary of safety can be found in [Appendix 2.7.1: 1] and in [Sec. 2.7.2.3.4].

2.1.2 Multiple Dose Pharmacokinetic Study (PN291)

This study was an open label, 3-period, randomized, multiple-dose study in 24 healthy, adult male and female subjects to evaluate the pharmacokinetics of 1200 mg QD (as 3 x 400 mg tablets or 2 x 600 mg tablets) and 400 mg BID, each administered in the fasted state for 5 days. There was at least a 4-day washout in between treatment periods. Blood samples were collected for up to 24 hours following each dose administration of study drug on Days 1 and 5.

Administration of the 1200 mg dose given as 2 x 600 mg tablets once daily resulted in a GM (CV%) C_{trough} of 81.1 nM (72%), $AUC_{0\text{-}24}$ of 59.5 µM-hr (34%), and C_{max} of 20.6 µM (44%) on Day 5. Multiple daily doses of 1200 mg given as 2 x 600 mg tablets resulted in no accumulation in $AUC_{0\text{-}24}$ and C_{max} on Day 5 relative to Day 1, and PK parameter values

observed in this study on Day 5 were similar to those observed in the single dose food effect study (fasted) (PN290).

Administration of the 1200 mg dose given as 3 x 400 mg tablets once daily resulted in a GM (CV%) C_{trough} of 83.5 nM (53%), AUC_{0-24hr} of 49.0 µM-hr (73%), and C_{max} of 14.1 µM (99%) on Day 5. Multiple daily doses of 1200 mg given as 3 x 400 mg tablets resulted in little to no accumulation of AUC_{0-24} or C_{max} after 5 days of administration.

Administration of the 400 mg dose given twice daily resulted in a GM (CV%) C_{trough} of 130.9 nM (56%), AUC_{0-24} (2 x AUC_{0-12}) of 25.4 µM-hr (106%), and C_{max} of 3.4 µM (153%) on Day 5. Multiple twice-daily doses of the 400 mg tablet resulted in no accumulation of AUC or C_{max} after 5 days of administration.

The study of multiple dose pharmacokinetics of raltegravir revealed predictable pharmacokinetics with regard to accumulation and steady state.

A summary of safety can be found in [Appendix 2.7.1: 1] and in [Sec. 2.7.2.3.4].

3 COMPARISON AND ANALYSES OF RESULTS ACROSS STUDIES

3.1 Relative Bioavailability - Formulation Selection

Two formulations were considered for the feasibility of once daily dosing: the existing marketed 400 mg tablet and a 600 mg tablet. Data from the Phase 1 studies PN290 and PN291, which provided the relevant biopharmaceutic characterization of the formulations in fasted and fed states, and PN293 (reviewed in [Sec. 2.7.2]), which provided safety and pharmacokinetic experience at a dose higher than 1200 mg, together with modeling and simulation, resulted in selection of the 600 mg formulation (1200 mg dose [as 2 x 600 mg tablets]) for further evaluation as once daily dosing in PN292.

Results from PN290 and PN291 demonstrated that raltegravir 1200 mg QD (2 x 600 mg) has a higher bioavailability compared to the 400 mg formulation (1200 mg administered as 3 x 400 mg tablets): following single doses, AUC_{inf} was 63% higher for 1200 mg QD (2 x 600 mg) [Ref. 5.3.1.1: P290], and following multiple doses, AUC_{0-24} was 21% higher for 1200 mg QD (2 x 600 mg) [Ref. 5.3.1.1: P291]. These results are consistent with in vitro dissolution tests. Administration of raltegravir 1200 mg QD (2 x 600 mg) results in a higher daily AUC and C_{max} compared to administration of the 400 mg formulation BID: following multiple doses, AUC_{0-24} and C_{max} were 2.3-fold and 6.0-fold higher, respectively, for 1200 mg QD compared to 400 mg BID [Ref. 5.3.1.1: P291]. This is consistent with the differences in the total daily dose (1200 mg compared with 800 mg) and the somewhat higher bioavailability with the 600 mg tablet. Based on study results from PN290, the food effect observed with 1200 mg QD administered as 2 x 600 mg tablets is also less than that observed with the 400 mg formulation (1200 mg administered as 3 x 400 mg tablets).

As part of the tablet strength (400 mg vs. 600 mg) selection for Phase 3 evaluation, the PK/PD viral dynamics model previously developed using data from QDMRK (PN071) was updated with data from PN290 and PN291, to project the probability of achieving non-inferiority for the two different tablet strengths (400 mg and 600 mg) when used in a dose of

1200 mg QD. Details of the modeling and simulation and results in support of the dose selection are described in [Sec 2.7.2.2.2.5]. The potential of food effect was also taken into consideration for the final formulation selection, with details described in [Sec 2.7.1.3.2]. Overall, the PK/PD simulation supported the selection of the 600 mg tablet (used in a 1200 mg QD dose [as 2 x 600 mg tablets]) to take forward into the Phase 3 study, PN292. The appropriateness of this dose and formulation were confirmed in PN292, which demonstrated non-inferior efficacy and comparable safety for 1200 mg QD compared to 400 mg BID.

3.2 Assessment of a Food Effect

The effect of food on the pharmacokinetics of raltegravir may be due to a combination of factors (e.g., altered pH dependent solubility of raltegravir, changes in gastric retention or complex formation) that influence the *in vivo* dissolution of the drug product and absorption of the drug substance. The effect of food on raltegravir pharmacokinetics is variable depending on meal type, and this is true of both the 600 mg tablet and the 400 mg tablet. Based on results from PN290, administration of a low-fat meal with raltegravir 1200 mg (2 x 600 mg) resulted in a 42% decrease in $AUC_{0\text{-last}}$, 52% decrease in C_{max}, and 16% decrease in C_{24hr}. Administration of a high-fat meal resulted in a 1.9% increase in $AUC_{0\text{-last}}$, 28% decrease in C_{max}, and 12% decrease in C_{24hr}. The magnitude of this food effect was less than that observed for the 400 mg tablet administered as 1200 mg (3 x 400 mg) in the same study: administration of a low-fat meal resulted in a 73% decrease in $AUC_{0\text{-last}}$, 75% decrease in C_{max}, and 18% decrease in C_{24hr}. Administration of a high-fat meal resulted in a 39% increase in $AUC_{0\text{-last}}$, 23% decrease in C_{max}, and 70% increase in C_{24hr}. The favorable food effect with the 600 mg tablet is in part due to the lower variability and higher exposure.

The impact of food on the exposure-efficacy relationship of raltegravir 1200 mg QD (2 x 600 mg) was evaluated via viral dynamics modeling, described in [Sec 2.7.2.2.2.5]. A variety of dosing conditions were evaluated: raltegravir 1200 mg QD (as 2 x 600 mg tablets) in the fasted state, with a low-fat meal, or with a high-fat meal; these were compared with 400 mg BID (1 x 400 mg tablet) given with different meal types for the 2 daily doses (e.g., taken with a low-fat meal in the morning, but with a high-fat meal in the evening). As shown in [Table 2.7.1: 4], the simulated efficacy for 1200 mg QD (2 x 600 mg) is comparable to 400 mg BID under a variety of food conditions, including scenarios where raltegravir is taken primarily with a low-fat meal. These results further confirmed that the effect of food on raltegravir pharmacokinetics is not clinically significant.

Table 2.7.1: 4

Viral Dynamics Model Projections of the Probability of Achieving Non-inferiority of Raltegravir 1200 mg QD Relative to Raltegravir 400 mg BID (1 x 400 mg tablet) in a Phase 3 Study (10% NI margin; N=345/arm), Assuming Doses are Taken Consistently Under the Listed Food Conditions (Based on Observed Data from PN290 Extrapolated to Steady State)

Raltegravir Regimen / Meal Type		Raltegravir 400 mg BID					
		1st fasted 2nd fasted	1st low-fat 2nd low-fat	1st high-fat 2nd high-fat	1st fasted 2nd low-fat	1st fasted 2nd high-fat	1st low-fat 2nd high-fat
1200 mg QD (2 x 600 mg)	Fasted	90%	-	-	>95%	85%	-
	Low-fat	-	>95%	-	>95%	-	94%
	High-fat	-	-	85%	-	94%	>95%
1200 mg QD (3 x 400 mg)	Fasted	92%	-	-	>95%	88%	-
	Low-fat	-	86%	-	66%	-	62%
	High-fat	-	-	>95%	-	>95%	>95%

Data Source: [Ref. 5.3.5.3: 04CNKQ]

Because raltegravir 1200 mg QD (as 2 x 600 mg tablets) provided more robust simulated efficacy in all three scenarios of the fasted state, with a low-fat meal, and with a high-fat meal, when compared with 1200 mg QD (as 3 x 400 mg tablets), raltegravir 1200 mg as 2 x 600 mg was taken forward for further development. The 1200 mg QD presentation as 3 x 400 mg tablets was discontinued from further development.

The pooled dataset from Phase 1 and Phase 3 studies in the Once Daily Development program provided an opportunity to characterize and better understand the impact of food and different meal types (including moderate-fat that was not investigated in PN290) on the absorption kinetics of raltegravir using population PK modeling [Ref. 5.3.5.3: 04C39T]. A lag time for doses administered with food was necessary to capture the onset of raltegravir absorption profile, which was approximately 11 minutes. The duration of the sigmoid absorption and bioavailability were dependent on meal type. Duration of absorption for raltegravir was estimated to be 29 minutes, 1.32 hours, and 3.15 hours for doses administered fasted, with low- or moderate-fat meals, and high-fat meals, respectively. Raltegravir bioavailability administered with a low-fat or moderate-fat meal was 75.6% and 85.4% relative to fasted condition, respectively. When administered with a high-fat meal, raltegravir bioavailability approached that of the fasted condition. Overall, food effect results from population PK modeling demonstrated consistency with the observed impact of the different meal types (low-fat and high-fat) on raltegravir PK from PN290, and provided additional understanding on the impact of moderate-fat on raltegravir PK. In PN292, raltegravir 1200 mg QD was administered without regard to food or meal type, and the study results confirmed robust efficacy and favorable safety, supporting the recommendation of dosing of 1200 mg QD (2 x 600 mg) without regard to food.

Overall, similar to raltegravir 400 mg BID, the observed food effect on raltegravir 1200 mg QD (2 x 600mg) increased raltegravir PK variability, but the magnitudes of these effects are not considered clinically meaningful. The totality of the results support the recommendation in the proposed labeling for dosing without regard to food for raltegravir 1200 mg QD (as 2 x 600 mg tablets), as is currently instructed for raltegravir 400 mg BID.

4 CONCLUSIONS

1. The raltegravir 600 mg tablet for once-daily use is a non-poloxamer based film-coated dosage form, different from the 400 mg tablet by higher drug loading and better processability. Non-functional film coat composition differences between the 600 mg tablet used in Phase 3 and the FMI were bridged with in vitro dissolution data in line with appropriate regulatory guidelines. The dissolution profile of the raltegravir 600 mg tablet showed a profile that was consistent with that of an immediate release dosage form. Overall, the in vivo performances of the dosage forms were consistent with their in-vitro dissolution profile.

2. The biopharmaceutics of raltegravir 1200 mg QD, characterized in two Phase 1 studies (PN290 and PN291) along with the extensive PK/PD modeling and simulations, supported that a dose of raltegravir 1200 mg QD (2 x 600 mg) would have the fasted and fed pharmacokinetic profile necessary for efficacy with once daily administration without regard to food. Specifically with respect to food effect, PN290 demonstrated that the 600 mg tablet had similar or smaller food effects when studied under high-fat and low-fat meal conditions when compared to the 400 mg tablet. The suitability of the 600 mg tablet for raltegravir QD dosing was further confirmed in the Phase 3 study PN292.

5 APPENDIX

Appendix 2.7.1: 1

Biopharmaceutic Studies in the Raltegravir Once Daily Development Program

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range (yr)				
Module 5.3.1 Biopharmaceutic Studies								
Module 5.3.1.1 Bioavailability Studies								
P290	Evaluate the single dose food effect on the pharmacokinetics of raltegravir once-daily.	20	16	20-55	Raltegravir 1200 mg (2 x 600 mg tablets) single dose	[redacted]	**Pharmacokinetic:** The pharmacokinetic (PK) parameters AUC_{0-last}, AUC_{0-inf}, C_{max}, C_{24hr}, T_{max}, K_{el} and T_{half} were estimated using a non-compartmental approach. **Safety:** Safety evaluations included clinical assessment of tolerability, physical examinations, vital signs, 12-lead electrocardiogram, laboratory safety tests (chemistry, hematology, urinalysis), and evaluation of adverse experiences.	**Pharmacokinetic:** <u>1200 mg dose as 2 x 600 mg</u> ▪ Fasted: GM (CV%) C_{24hr} of 57.7 nM (44%), C_{max} of 22.6 µM (43%), and AUC_{0-last} of 56.5 µM-hr (38%). ▪ Low Fat Meal: 42% decrease in AUC_{0-last}, 52% decrease in C_{max}, and 16% decrease in C_{24hr}. ▪ High Fat Meal: 1.9% increase in AUC_{0-last}, 28% decrease in C_{max}, and 12% decrease in C_{24hr}. <u>1200 mg dose as 3 x 400 mg</u> ▪ Fasted: GM (CV%) C_{24hr} of 46.7 nM (31%), C_{max} of 9.2 µM (87%), and AUC_{0-last} of 33.8 µM-hr (66%). ▪ Low Fat meal: 73% decrease in AUC_{0-last}, 75% decrease in C_{max}, and 18% decrease in C_{24hr}. ▪ High Fat Meal: 39% increase in AUC_{0-last}, 23% decrease in C_{max} and 70% increase in C_{24hr}.
					Raltegravir 1200 mg (3 x 400 mg tablets) single dose	[redacted]		

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range (yr)				
Module 5.3.1 Biopharmaceutic Studies								
								Safety: ▪ The 1200 mg dose as 2 x 600 mg and 3 x 400 mg formulations were generally well-tolerated throughout the study. ▪ There were no serious or severe clinical or laboratory adverse events reported during the treatment portion of the study and no subjects were discontinued from the study due to an adverse experience. ▪ There was no apparent relationship between the frequency and intensity of adverse experiences and the dose of the 600 mg and 400 mg tablets. ▪ Blood chemistry, hematology, ECG and vital sign parameters were monitored throughout the study and no clinically meaningful changes from baseline values were observed.

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range (yr)				
Module 5.3.1 Biopharmaceutic Studies								
P291	Evaluate the multiple-dose pharmacokinetics of raltegravir once daily	16	8	25-55	Raltegravir 1200 mg (2 x 600 mg tablets once daily) x 5 days	[redacted]	**Pharmacokinetic:** The pharmacokinetic (PK) parameters AUC_{0-24} /AUC_{0-12}, C_{max}, C_{trough} (C_{24hr}/C_{12hr}) and T_{max} were estimated using a non-compartmental approach. **Safety:** Safety evaluations included clinical	**Pharmacokinetic:** <u>1200 mg dose as 2 x 600 mg QD x 5 Days</u> ▪ Day 5: GM (CV%) C_{trough} of 81.1 nM (72%), AUC_{0-24} of 59.5 µM-hr (34%), and C_{max} of 20.6 µM (44%). ▪ Multiple daily doses resulted in no accumulation in AUC_{0-24} and C_{max} on Day 5 relative to Day 1, and PK parameter values observed in this study on Day 5 were similar to those observed

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range (yr)				
Module 5.3.1 Biopharmaceutic Studies								
					Raltegravir 1200 mg (3 x 400 mg tablets once daily) x 5 days. Raltegravir 800 mg (1 x 400 mg tablets twice daily) x 5 days	[redacted]	assessment of tolerability, physical examinations, vital signs, 12-lead electrocardiogram, laboratory safety tests (chemistry, hematology, urinalysis), and evaluation of adverse experiences.	in the single dose study (fasted) PN290. <u>1200 mg dose as 3 x 400 mg QD x 5 Days</u> ▪ Day 5: GM (CV%) C_{trough} of 83.5 nM (53%), AUC_{0-24hr} of 49.0 µM-hr (73%), and C_{max} of 14.1 µM (99%). ▪ Multiple daily doses resulted in little to no accumulation of AUC or C_{max} after 5 days of administration. <u>400 mg dose as 1 x 400 mg BID x 5 Days</u> ▪ Day 5: GM (CV%) C_{trough} of 130.9 nM (56%), AUC_{0-24} (2 x AUC_{0-12}) of 25.4 µM-hr (106%), and C_{max} of 3.4 µM (153%). ▪ Multiple twice-daily doses resulted in no accumulation of AUC or C_{max} after 5 days of administration.

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range (yr)				
Module 5.3.1 Biopharmaceutic Studies								
								Safety: ▪ The 1200 mg dose as 2 x 600 mg and 3 x 400 mg formulations were generally well-tolerated throughout the study. ▪ There were no serious or severe clinical or laboratory adverse events reported during the treatment portion of the study and no subjects were discontinued from the study due to an adverse experience. ▪ There was no apparent relationship between the frequency and intensity of adverse experiences and the dose of the 600 mg and 400 mg tablets. ▪ Blood chemistry, hematology, ECG and vital sign parameters were monitored throughout the study and no clinically meaningful changes from baseline values were observed.

Data Source: [Ref. 5.3.1.1: P290, P291]

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

1 BACKGROUND AND OVERVIEW

Raltegravir (also known as ISENTRESS® MK-0518, and [redacted]) is a human immunodeficiency virus (HIV)-1 integrase strand transfer inhibitor with potent in vitro activity against HIV-1, exhibiting a 95% inhibitory concentration (IC_{95}) of 33 nM in the presence of 50% human serum, and currently marketed for twice daily (BID) use. Raltegravir for once daily (QD) use offers a new option for the initial treatment of HIV-1 infected subjects. As described in this 48 Week Once Daily Application (referred to as the Once Daily Application), raltegravir for once daily use, in combination with emtricitabine and tenofovir, was highly efficacious and well tolerated among treatment-naïve HIV-1 infected subjects.

Across this summary document [Sec. 2.7.2], references to the raltegravir 400 mg tablet pertain to the marketed ISENTRESS® 400 mg film-coated tablet currently registered for twice daily use and references to the raltegravir 600 mg tablet (or 1200 mg QD not otherwise specified) pertain to the 600 mg film-coated tablet formulation developed for once daily dosing.

Original Application

In the Original Application for raltegravir at a dose of 400 mg BID, data were presented regarding the safety, tolerability, and pharmacokinetic profile of raltegravir from Phase 1 studies conducted in healthy, male and female subjects and special populations. Raltegravir was found to be primarily eliminated by metabolism via glucuronidation mediated by uridine diphosphate glucuronosyltransferase (UGT) 1A1. Raltegravir displays dose proportional pharmacokinetics over the dose range of 100 to 1200 mg. At the current marketed dose of 400 mg BID, the apparent terminal elimination half-life is approximately 9 hours with a shorter α-phase half-life (~1 hour) accounting for much of the area under the concentration time curve (AUC). Steady-state is generally reached in 2 days, and accumulation is minimal with multiple-dose administration; the estimated AUC accumulation ratio is 1.05 with twice daily dosing. Raltegravir is relatively rapidly absorbed with a median time to maximum plasma concentration (T_{max}) of ~3 hours in the fasted state. Administration of raltegravir with food has a variable effect on the pharmacokinetics, but the food effect is not clinically meaningful and 400 mg BID raltegravir can be administered without regard to food. Gender, age, body mass index, race, and HIV status had no clinically meaningful effect on raltegravir pharmacokinetics. Moderate hepatic insufficiency and severe renal insufficiency also had no clinically meaningful effect on raltegravir pharmacokinetics. No dose adjustment is required for raltegravir based on these demographic factors.

Data from a number of drug interaction studies were presented in the Original Application, including assessment of raltegravir as a victim or as a perpetrator of drug interactions. Raltegravir has a low propensity to be involved in drug-drug interactions (DDIs) either as a victim or as a perpetrator. In vitro, raltegravir is not a potent inhibitor or inducer of major drug metabolizing enzymes. In addition, raltegravir is not a potent inhibitor of human drug efflux and uptake transporters in vitro [Ref. 5.4: 03Z7Q3]. Raltegravir does not meaningfully alter the pharmacokinetics of midazolam, providing evidence that raltegravir has a low propensity for perpetrating drug interactions with substrates of CYP3A4. Additionally,

raltegravir does not meaningfully alter the pharmacokinetics of tenofovir, etravirine, and lamivudine. Raltegravir is not a substrate of CYP enzymes and therefore, it is not expected to be a victim of DDI via CYP inhibition or induction. Based on in vivo and in vitro studies, raltegravir is eliminated mainly by metabolism via a UGT1A1-mediated glucuronidation pathway and coadministration of UGT1A1 inhibitors or inducers may alter plasma levels of raltegravir. In general, use of raltegravir 400 mg BID is not recommended with aluminum/magnesium hydroxide-containing antacids, and a dose increase to 800 mg BID is sometimes used during coadministration with rifampin (e.g., in the US).

Once Daily Application

In this Once Daily Application, data are presented showing that raltegravir at a dose of 1200 mg QD (2 x 600 mg tablets for once daily use) is rapidly absorbed with median T_{max} ~1.5 to 2 hours in the fasted state and generates a sharper absorption peak with a tendency to achieve a higher C_{max} in comparison to raltegravir BID (1 x 400 mg tablet twice daily). In addition, the raltegravir 600 mg tablet formulation has higher dose-normalized systemic exposure (AUC_{0-24}/dose increased by approximately 21-66%) compared with the raltegravir 400 mg tablet formulation. In general, the food effect observed for raltegravir 1200 mg QD (2 x 600 mg), particularly with high-fat meal, is less than that observed for the 400 mg BID formulation and is not clinically meaningful (see [Sec. 2.5.2] and [Sec. 2.7.1.3.2] for further discussion of food effect). Once absorbed, both formulations of raltegravir exhibit similar systemic pharmacokinetics. The apparent terminal elimination half-life is approximately 9 to 12 hours with a shorter α-phase half-life (~1 hour) accounting for much of the AUC. Steady-state is generally reached in 2 days, with little to no accumulation with multiple dose administration.

Intrinsic (e.g., gender, race) and extrinsic factor (e.g., drug interactions) effects on the pharmacokinetics of raltegravir 1200 mg (2 x 600 mg) QD were assessed through a combination of Phase 1 studies, population PK analysis in a pooled dataset containing data from Phase 1 studies and the Phase 3 study PN292. Findings from these analyses were largely consistent with historical data from the raltegravir twice daily development program. Exposure-efficacy analysis was conducted to evaluate the PK/PD relationship for raltegravir 1200 mg QD and confirm its consistency with previous conclusions made for ISENTRESS® 400 mg BID. Exploratory exposure-safety analysis was also conducted and this information along with the overall understanding of raltegravir exposure-efficacy characteristics were used to define clinical comparability bounds that were then used to assess the clinical relevance of the identified intrinsic and extrinsic factor effects. Population PK modeling and simulation analyses were conducted to identify an appropriate weight cut-off at which raltegravir 1200 mg QD (2 x 600 mg) can be administered in the pediatric population.

1.1 General Background on the Clinical Pharmacology Program

The Once Daily Development Program included six Phase 1 studies (see [Table 2.5: 1]) which enrolled male and female healthy subjects and subjects with HIV infection and characterized the safety and tolerability as well as pharmacokinetic and drug interaction characteristics of raltegravir 1200 mg (2 x 600 mg) QD. Two of the Phase 1 studies (PN290 and PN291) that assessed the biopharmaceutic properties of raltegravir QD are presented in

[Sec. 2.7.1] and the remaining four Phase 1 studies (PN293, PN812, PN823, PN824) are presented in [Sec. 2.7.2], along with an integrated assessment of safety and tolerability from all six Phase 1 studies [Sec. 2.7.2.3.4]. Raltegravir 1200 mg QD (2 x 600 mg) pharmacokinetics and pharmacodynamics using data from Phase 1 and Phase 3 studies were further evaluated using population pharmacokinetic modeling [Sec. 2.7.2.2.2.1], and exposure-response analysis [Sec. 2.7.2.2.2.2] and [Sec. 2.7.2.2.2.3], to support the final clinical dose selection. Modeling and simulation performed to identify an appropriate weight cut-off at which raltegravir 1200 mg QD (2 x 600 mg) can be safely administered in the pediatric population is described in [Sec. 2.7.2.3.2.2.1].

1.1.1 Pharmacokinetics of Once-Daily Raltegravir

Absorption

Raltegravir 1200 mg QD (2 x 600 mg tablets) is rapidly absorbed with a median T_{max} of approximately 1.5 to 2 hours in the fasted state. Relative to both raltegravir 400 mg BID (2 x 400 mg tablets) and raltegravir 1200 mg QD (3 x 400 mg tablets), raltegravir 1200 mg QD (2 x 600 mg tablets) has higher systemic exposure (AUC_{0-24} increased by approximately 21-66% compared with 1200 mg QD [3 x 400 mg tablets] and 2.3-fold compared to 400 mg BID) using data from PN290 and PN291. Steady-state exposure is generally reached in 2 days, with little to no accumulation with multiple dose administration.

In study PN290, single dose administration of raltegravir 1200 mg QD (2 x 600 mg tablets) with a low-fat meal resulted in a 42% decrease in AUC_{0-last}, 52% decrease in C_{max}, and 16% decrease in C_{24hr}, compared to administration in the fasted state. Administration of raltegravir 1200 mg QD (2 x 600 mg tablets) with a high-fat meal resulted in a 1.9% increase in AUC_{0-last}, 28% decrease in C_{max}, and 12% decrease in C_{24hr}. The effect of food on raltegravir 1200 mg QD (2 x 600 mg tablets) was smaller than the food effect observed for the 400 mg tablet administered as 1200 mg (3 x 400 mg) in the same study. Overall, the food effect is not expected to be clinically meaningful, thus, raltegravir 1200 mg QD (2 x 600 mg tablets) can be administered with or without food, as further discussed in [Sec. 2.7.1.3.2].

Distribution

Raltegravir is moderately bound (83%) to proteins in human plasma in vitro. Raltegravir does not significantly partition into human blood cells in vitro, with a blood-to-plasma concentration ratio of 0.6. In vitro studies show that raltegravir is a P-glycoprotein (P-gp) substrate.

Elimination

The major elimination pathway of raltegravir is via UGT 1A1-mediated glucuronidation. Similar to the raltegravir 400 mg BID formulation, the apparent terminal elimination half-life of the 600 mg tablet formulation is approximately 9 to 12 hours with a shorter α-phase half-life (~1 hour) accounting for much of the AUC.

Instrinsic factors and special populations

The impact of body weight, race, ethnicity, gender, and HIV infection on the pharmacokinetics of raltegravir 1200 mg QD (2 x 600 mg tablets) were evaluated by population pharmacokinetic analysis, all of which did not have clinically meaningful impact on raltegravir PK [Sec. 2.7.2.3.2]. In addition, while raltegravir 1200 mg (2 x 600 mg) was not evaluated in a pediatric clinical study, population PK modeling and simulation analyses were conducted and support the use of raltegravir 1200 mg QD in pediatric patients weighing at least 40 kg [Sec. 2.7.2.2.2.4], [Sec. 2.7.2.3.2.2.1].

Extrinsic factors –Drug-Drug Interactions (DDIs)

Findings from in vitro metabolism and transporter studies conducted in support of the raltegravir 400 mg BID regimen can be extended to the raltegravir 600 mg formulation used in the once daily dosing regimen. Raltegravir is not a substrate of cytochrome P450 (CYP) enzymes and therefore, it is not expected to be a victim of DDIs via CYP inhibition or induction. In vitro, raltegravir is not an inhibitor of the major CYP isozymes, nor an inducer of CYP1A2, CYP2B6 or CYP3A4. Raltegravir does not meaningfully alter the pharmacokinetics of midazolam, providing evidence that it has a low propensity for perpetrating drug interactions with substrates of CYP3A4. Similarly, raltegravir is not a potent inhibitor of UGT1A1, UGT2B7 or major drug transporters in vitro [Sec. 2.7.2.1.2]. Thus, the propensity for raltegravir to perpetrate DDIs with substrates of the above enzymes or transporters at clinically relevant exposures is low.

Based on previous clinical experience with raltegravir 400 mg BID, coadministration of raltegravir with metal-cation antacids, drugs that alter gastric pH, and drugs that potently inhibit or induce UGT1A1 may affect plasma levels of raltegravir. Therefore, three DDI studies were performed in the Once Daily Development Program; these studies included a raltegravir/efavirenz interaction study in healthy volunteers (PN812), a raltegravir/atazanavir interaction study in healthy volunteers (PN823), and a raltegravir/antacid interaction study in HIV-infected subjects (PN824). Efavirenz, a known moderate UGT1A1 inducer, was selected to assess whether decreases in raltegravir pharmacokinetics at a dose of 1200 mg (2 x 600 mg tablets) were clinically meaningful when coadministered with moderate inducers. Efavirenz modestly reduced the exposure of raltegravir 1200 mg QD (Raltegravir $AUC_{0-\infty}$, C_{max}, and C_{24} were decreased 14%, 9%, and 6%, respectively, when co-administered with efavirenz compared to when raltegravir was administered alone; for results see [Sec. 2.7.2.3.3.1.2]); however, these changes are not considered to be clinically meaningful, thus coadministration is permitted. Atazanavir, a known inhibitor of UGT1A1, was selected to assess the expected upper limit of increases in the pharmacokinetics of a single dose of raltegravir 1200 mg (2 x 600 mg tablets) anticipated due to drug interactions. Atazanavir significantly increased the exposure of raltegravir 1200 mg QD (1.67- and 1.16-fold increases in raltegravir $AUC_{0-\infty}$ and C_{max}, respectively, when co-administered with atazanavir compared to when raltegravir was administered alone; for results see [Sec. 2.7.2.3.3.1.2]), thus coadministration is not recommended. Binding of the metal-binding motif in raltegravir with the divalent metal cations contained in some antacids has been shown to result in decreased raltegravir absorption and diminished raltegravir plasma concentrations when coadministered. Coadministration of raltegravir 1200 mg QD (2 x 600 mg tablets) with

aluminum/magnesium and calcium carbonate containing antacids reduced the exposure to raltegravir 1200 mg QD significantly (up to 72% decrease in raltegravir exposures when calcium carbonate antacid was given with raltegravir concomitantly and up to 57% decrease in raltegravir exposure when the calcium carbonate antacid was spaced by 12 hours with raltegravir, and up to 58% decrease in exposures when aluminium/magnesium hydroxide antacid was spaced by 12 hours with raltegravir; for results see [Sec. 2.7.2.3.3.1.2]); thus, coadministration of aluminium/magnesium and calcium carbonate antacids (concomitantly or staggered by 12 hours) with raltegravir 1200 mg QD is not recommended.

Furthermore, population pharmacokinetic analysis was used to evaluate the impact of concomitant use of raltegravir 1200 mg QD (2 x 600 mg) with TRUVADA™, proton-pump inhibitors (PPIs) and H2 blockers. Results from these analyses are described in [Sec. 2.7.2.3.3]. Tenofovir, a componenent of TRUVADA™, has been shown to increase raltegravir exposure when coadministered with raltegravir 400 mg BID [Ref. 5.4: 03QMY6]. H2 blockers and PPIs, both which increase gastric pH, could increase raltegravir solubility, and thus elevate raltegravir plasma concentrations. Concomitant use of TRUVADA™, H2 blockers, and PPIs was permitted within PN292. Overall, TRUVADA™, PPIs and H2 blockers were not found to impact raltegravir PK in a clinically meaningful manner, thus coadministration is permitted.

The impact of rifampin (a strong inducer of drug metabolizing enzymes, including UGT1A1) on raltegravir 1200 mg QD is unknown, but coadministration is likely to decrease raltegravir trough levels based on the significant reduction in trough concentrations observed with raltegravir 400 mg BID; thus coadministration is not recommended. The impact of other strong inducers of drug metabolizing enzymes, such as phenytoin and phenobarbital, on UGT1A1 is unknown, therefore coadministration with raltegravir 1200 mg QD is not recommended. The impact of tipranavir/ritonavir on raltegravir 1200 mg QD is unknown, but co-administration is likely to significantly decrease raltegravir trough levels, thus coadministration is not recommended. Detailed are described in [Sec. 2.7.2.3.3.1.2].

1.1.2 Pharmacodynamics

Pharmacodynamics following once daily dosing of raltegravir were not assessed in the Phase 1 Once Daily Development Program.

1.1.3 Safety

The overall safety evaluation plan for each Phase 1 study is described in the respective clinical study reports [Ref. 5.3.1.1: P290, P291] [Ref. 5.3.2.2: P812, P823, P824] [Ref. 5.3.3.1: P293]. An integrated summary of safety from all six Phase 1 studies is provided in [Sec. 2.7.2.3.4] and [Sec. 5.3.5.3.3]. Overall, raltegravir was generally well tolerated at doses as high as 1800 mg (administered as 3 x 600 mg tablets) once daily for 28 days. Across all six studies, there were a total of four serious adverse events (chest pain, dyspnoea, orthostatic hypotension and rash), all reported by a single subject in the raltegravir /antacid interaction study in HIV-infected subjects (PN824). All other adverse events observed across the Phase 1 studies were generally transient and mild to moderate in intensity. There were a total of three discontinuations due to the study drug. Of the

three subjects who discontinued due to adverse experiences, one subject received raltegravir alone and two subjects received efavirenz or atazanavir alone, respectively. No clinically important abnormalities were noted in routine blood and urine chemistry panels, complete blood count (CBC), electrocardiograms (ECGs), and physical examinations including vital signs, except in PN293, the 28-day safety study of raltegravir 1800 mg (3 x 600 mg). Drug related liver transaminase elevations were seen when raltegravir 1800 mg QD was given for 28 days in PN293. One subject experienced ALT >3x ULN and one subject experienced ALT >2x ULN; both were in the raltegravir treatment group. Both subjects' ALT returned to normal range while continuing on raltegravir treatment. Total and direct bilirubin levels were WNL throughout the study dosing period. The liver transaminase elevations had no apparent relationship with PK exposure and were not considered clinically significant. Five subjects showed elevations in CPK; however, four of the five did not show elevations until after the dosing had been completed and the subjects were no longer domiciled. Of the five subjects, two experienced CPK >20 x ULN and one experienced ~9 x ULN; for these three subjects, the intensity of the event was rated as severe by the investigator and was considered related to the study drug.

Three subjects showed QTc values that were out of range in PN291, a 5-day multiple 1200 mg dose study; these were rated mild in severity and were considered possibly related to the study drug. A thorough QTc study (PN024) was previously performed as part of the raltegravir twice daily development program and the data were included in a prior submission (see Original Application). The single supra-therapeutic 1600 mg dose did not prolong the QTc interval. Enhanced ECG monitoring in PN293 at the 1800 mg dose showed no meaningful trends on QTc.

For a description of the exposure - safety analysis, refer to [Sec. 2.7.2.1.3.3].

1.2 Overview of In Vitro Human Biomaterial Studies

No new in vitro human biomaterial studies were conducted in support of this raltegravir Once Daily Application. Key raltegravir in vitro human data from previous submissions and publication by the Applicant are summarized below.

Raltegravir is moderately bound (83%) to proteins in human plasma in vitro. The in vitro blood-to-plasma concentration ratio of raltegravir is 0.6, indicating that raltegravir does not significantly partition into human blood cells.

In human hepatocytes, raltegravir is metabolized primarily via glucuronidation of the parent compound. Small quantities of the glucose conjugate of the parent compound and the acetyl hydrazine derivative are also detected. In vitro studies identified UGT1A1 as the primary enzyme catalyzing the glucuronidation of raltegravir.

Raltegravir does not inhibit (IC_{50}>100 μM) CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 and CYP3A or induce CYP1A2, CYP2B6 and CYP3A4 in vitro. In addition, raltegravir is not a potent inhibitor (IC_{50}>50 μM) of the UGTs tested (UGT1A1, UGT2B7).

Raltegravir is a substrate of P-gp, but does not inhibit P-gp in vitro over a concentration range of 1 to 100 µM. Similarly, raltegravir showed only 22% inhibition of breast cancer resistance protein (BCRP)-mediated transport at 100 µM. Raltegravir does not inhibit organic anion transporting polypeptide (OATP) 1B1, and it showes 40% inhibition of OATP1B3 and minimal inhibition (16%) of organic cation transporter (OCT)1 at 100 µM in vitro. Raltegravir does not inhibit OCT2 and it is not a potent inhibitor of organic anion transporter (OAT)1 and OAT3 (IC_{50} of 108 µM and 18.8 µM, respectively), and multidrug and toxin extrusion proteins (MATE)1 and MATE2-K (52% and 29% inhibition at 100 µM, respectively) in vitro[Ref. 5.4: 03Z7Q3].

1.3 Overview of Dose Selection and Comparability Bounds Defining a Clinically Significant Change in Raltegravir Once Daily Pharmacokinetics

This section reviews the justification for the recommended dose of raltegravir 1200 mg QD (2 x 600 mg tablets) and the determination of the comparability bounds that define a clinically significant change in raltegravir pharmacokinetics, if exceeded (for upper bound) or not achieved (for lower bound). Results from the six Phase 1 studies and PN292 support that raltegravir 1200 mg QD (2 x 600 mg tablets) provides plasma concentrations within the range of concentrations generally associated with safe and effective treatment. The comparability bounds for clinically significant changes are determined based on the limits of departure from the typical 1200 mg QD exposures derived from PK data available from PN292 and Phase 1 studies of 1200 mg QD, as well as relevant information obtained from Protocol 071 (QDMRK, PN071), which was a prior Phase 3 study of raltegravir 800 mg QD (administered as 2 x 400 mg marketed tablets) versus raltegravir 400 mg BID.

The once daily raltegravir dose of 1200 mg (2 x 600 mg tablets) evaluated in the Phase 3 study PN292 was selected based on extensive analyses performed using a PK/PD viral dynamics model developed with data from Protocol 071 (QDMRK, PN071) and rich PK data from PN291. Results showed that a dose of 1200 mg QD (2 x 600 mg tablets) was projected to have efficacy similar to 400 mg BID, see [Sec. 2.7.2.1.3.1] and [Sec. 2.7.2.2.2.4] for additional details.

Based on results from PN292, raltegravir 1200 mg QD (2 x 600 mg tablets) demonstrated potent and statistically non-inferior antiretroviral activity and comparable immunological effect compared to raltegravir 400 mg BID at Week 48 (see [Sec. 2.5.4.2.4]). Raltegravir 1200 mg QD in PN292 demonstrated a favorable safety profile comparable with that of the 400 mg BID treatment group and consistent with the established safety profile of raltegravir twice daily (see [Sec. 2.5.5.2]). Overall, raltegravir 1200 mg QD has been generally well tolerated in the clinical program and no dose-related toxicities have been identified. Exposure-response analyses were also performed to evaluate the potential relationship between PK and efficacy [Sec. 2.7.2.2.2.2] and safety [Sec. 2.7.2.2.2.3]. Overall, results from these analyses further support the recommended raltegravir 1200 mg QD dose and the definition of a clinically meaningful change in the PK of raltegravir 1200 mg QD.

1.3.1 Selection of Raltegravir Doses for Evaluation in the Phase 3 Program

The safety and efficacy of once daily administration of raltegravir 800 mg QD (2 x 400 mg tablets) were previously evaluated in the Phase 3 trial PN071(QDMRK), which compared raltegravir 800 mg QD to raltegravir 400 mg BID, each in combination with TRUVADA™, in HIV-1 infected treatment-naïve patients. Both treatment arms (800 mg QD and 400 mg BID) demonstrated favorable tolerability and safety profiles. Despite high response rates in both arms, the 800 mg QD regimen failed to demonstrate non-inferiority to the 400 mg BID regimen at Week 48 with respect to the proportion of patients with HIV RNA <50 copies/mL (83.2% vs. 88.9%). Extensive PK/PD analyses were conducted on data from PN071 to enhance understanding of exposure-response relationships for raltegravir. This analysis included the PK parameters C_{trough} (concentration at the end of a dosing interval), C_{all} (average of all concentration values collected from sparse sampling, regardless of time of collection), and C_{min} (minimum concentration value collected from sparse sampling, regardless of time of collection), and the efficacy endpoints examined included HIV RNA <50 copies/mL, HIV RNA <400 copies/mL, and virologic failure. For patients in the 400 mg BID arm, there was no indication of any significant PK/PD association ($p<0.05$) over the range of tested PK values, which is consistent with prior analyses of PK/PD data after BID administration in the treatment-naïve population. In the analysis of the 800 mg QD arm, only one statistically significant relationship was identified (between C_{all} and HIV RNA <400 copies/mL); however, consistent trends in the expected direction were observed for each of the PK parameters and virologic endpoints. When data from both arms of the study were pooled, many significant relationships emerged, again trending in the expected directions. It was concluded from both quartile and Receiver Operating Characteristic (ROC) analyses that patients with C_{trough} values below 45 nM were at a higher risk of treatment failure, as this was the point where efficacy appeared to decline in the 800 mg QD arm [Ref. 5.4: 03RL43]. However, it should be noted that among patients with C_{trough} values below 45 nM only a slightly lower response rate (80%) for virologic efficacy was observed.

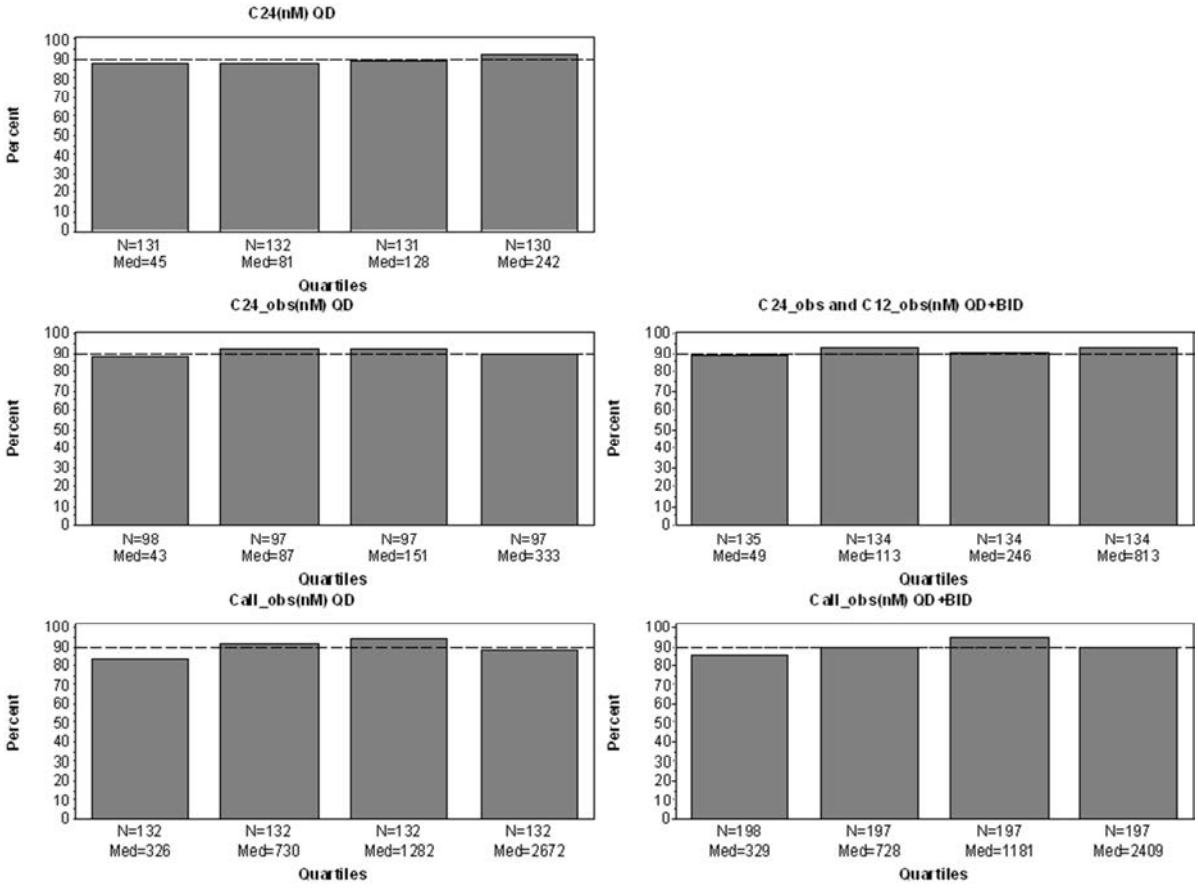
To further account for the effect of the raltegravir plasma concentration profile on efficacy, a PK/PD viral dynamics model was developed to project efficacy using data from the raltegravir 800 mg QD and 400 mg BID treatment arms of PN071 and short-term raltegravir monotherapy data from the Phase 2 study PN004. The model performed well in describing the outcomes observed in PN071 based on the PK profiles of 800 mg QD and 400 mg BID. Based on PK data from healthy volunteers receiving raltegravir 1200 mg QD (2 x 600 mg) from PN290 and PN291, it was projected, using the viral dynamics model, that a dose of 1200 mg QD (2 x 600 mg) would have efficacy similar to raltegravir 400 mg BID, and a high probability of demonstrating non-inferiority in a Phase 3 trial. The 1200 mg QD (2 x 600 mg) dose was expected to adequately increase raltegravir exposures (particularly C_{trough}) compared to the 800 mg QD dose, thus bringing the QD regimen closer to the BID regimen on the raltegravir exposure-efficacy curve. Therefore, raltegravir 1200 mg QD (2 x 600 mg) was chosen for evaluation in PN292. Details of the viral dynamics modeling and results are described in [Sec. 2.7.2.2.2.5].

1.3.2 Exposure-Response Relationships for Efficacy

The methodology described in [Sec. 2.7.2.2.2] was used to investigate the relationship between exposure and efficacy for the raltegravir 1200 mg QD (2 x 600 mg) dose and the raltegravir 400 mg BID dose in PN292. Three raltegravir exposure endpoints derived from sparsely sampled concentration data collected in PN292 were used for these analyses: C_{all_obs} (geometric mean of all observed concentrations for an individual patient, regardless of time of collection), C_{24_obs} and C_{12_obs} (geometric mean of the observed concentrations collected between 22 and 26 hours post-dose for 1200 mg QD, or 11 and 13 hours postdose for 400 mg BID), and C_{24} (steady state C_{24} values for subjects in the QD dosing arm, as derived from the population PK model).

For the analysis examining the potential relationship between raltegravir exposure and HIV-1 RNA<40 copies/mL (primary Phase 3 efficacy endpoint), neither baseline CD4 cell count nor Hepatitis B and/or C co-infection were significant in the covariate analysis. Since baseline viral load was previously shown to be a significant covariate in the exposure-response analysis from PN071 [Ref. 5.4: 03RL43] and screening viral load (≤100,000 or >100,000 copies/mL) was a significant covariate (p-value < 0.05) for some raltegravir exposure endpoints in this dataset [Ref. 5.3.5.3: 04C3B0], screening viral load was included as a covariate in the final logistic regression models for all PK endpoints. Overall, the odds ratios of PK and log-transformed PK parameters showed no statistical evidence of an association between any of the raltegravir exposure endpoints and probability of achieving HIV-1 RNA <40 copies/mL. Additionally, as shown in [Figure 2.7.2: 1], the percent of patients achieving HIV-1 RNA <40 copies/mL was evaluated by quartiles of the PK endpoints; these quartile analyses demonstrated no trend or apparent relationship between viral suppression and the range of raltegravir exposures achieved from both treatment regimens in PN292. It is important to note that, similar to ISENTRESS 400 mg BID and in contrast to 800 mg QD, a similar degree of viral suppression is achieved across all quartiles of the C_{trough} values from raltegravir 1200 mg QD, including the lowest quartile (< 25^{th} percentile). The increased degree of significance in the observed PK/PD relationships following pooled analysis of data from raltegravir 800 mg QD and 400 mg BID that was observed in the PN071 PK/PD analysis was not observed in the current analysis when raltegravir 1200 mg QD and ISENTRESS 400 mg BID data were pooled. This is likely due to the higher C_{trough} values observed from raltegravir 1200 mg QD relative to raltegravir 800 mg QD [Figure 2.7.2: 2]. The totality of these results suggests that maximum response was likely achieved across the raltegravir exposure range in PN292, including for 1200 mg QD, and is consistent with previous raltegravir PK/PD findings that demonstrated raltegravir data from ISENTRESS 400 mg BID is at the plateau region of the exposure-efficacy curve.

Figure 2.7.2: 1
Occurrence Rate of HIV-1 RNA Response Endpoint (<40 copies/mL) vs Quartiles of PK Parameters from Raltegravir 1200 mg QD and ISENTRESS 400 mg BID (dotted line = 90% response rate to achieving HIV RNA < 40 copies/mL; Med = median value in nM; C_{all_obs}=geometric mean of all observed concentrations for an individual patient, regardless of time of collection; C_{24_obs} and C_{12_obs} = geometric mean of the observed concentrations collected between 22 and 26 hours post-dose for 1200 mg QD, or between 11 and 13 hours postdose for 400 mg BID, respectively; and C_{24}=steady state C_{24} values for subjects in the QD dosing arm, as derived from the population PK model)



Data Source: [Ref. 5.3.5.3: 04C3B0]

For the analysis of change from baseline in CD4 cell count (secondary Phase 3 efficacy endpoint), no significant correlation was found for the majority of the PK endpoints from both raltegravir treatment regimens in PN292. In patients with screening HIV-1 RNA ≤100,000 copies/mL and hepatitis B and/or C co-infection, a trend (p-value <0.05) was observed between change from baseline in CD4 cell count and C_{all_obs} (Spearman's rank correlation = 0.645 and 0.497) for both raltegravir treatment regimens, and combined C_{trough} values (Spearman's rank correlation = 0.692) from both treatment regimens. However, due to the small sample size in these subgroups (N=11-13), no clinical significance can be concluded. Overall, no clinically meaningful correlations were found between raltegravir PK endpoints and change from baseline in CD4 cell counts, again supporting that the range of

raltegravir exposures attained in PN292 are likely on the maximal response plateau of the exposure-efficacy relationship.

1.3.3 Exposure-Response Relationships for Safety

No clinically meaningful adverse events that were related to raltegravir administration were observed in PN292 [Sec. 2.5.5]. Exploratory safety analyses based on raltegravir exposure quartiles were conducted, and details are described in [Sec. 2.7.2.2.2.3]. The raltegravir exposure endpoints used for these analyses were steady state AUC_{0-24} and C_{max} for each subject in PN292, determined using the population PK model described in [Sec. 2.7.2.2.2.1]. No significant difference was observed in the reports of clinical and laboratory adverse events in PN292 for subjects in the highest quartile of raltegravir exposure (69 µM*hr to 365 µM *hr for AUC_{0-24} and 20.5 µM to 48 µM for C_{max}) compared to subjects in the lower quartiles (16.5 to 69 µM*hr for AUC_{0-24} and 1.8 to 20.5 µM for C_{max}), and no trends were observed related to increasing raltegravir exposure across the quartiles [Table 2.7.4: 65], [Table 2.7.4: 66], [Table 2.7.4: 67], [Table 2.7.4: 68]. This confirmed the lack of any potential increased risks associated with the highest exposures from the raltegravir 1200 mg QD regimen.

1.3.4 Comparability Bounds Defining a Clinically Significant Change in Raltegravir Once Daily Pharmacokinetics

As discussed in the previous sections, efficacy of raltegravir 1200 mg QD reached the plateau region of the exposure-efficacy curve, similar to what was previously observed for ISENTRESS® 400 mg BID. Results from the safety-PK quartile analysis also confirmed the lack of association between raltegravir exposure and safety within the exposure range of the 1200 mg QD regimen. While these analyses confirmed acceptable efficacy and safety with administration of raltegravir 1200 mg QD, an integrated assessement with data from previous raltegravir experience was conducted to inform the clinical relevance of PK variability for the 1200 mg QD regimen, for example due to instrinsic or extrinsic factor effects.

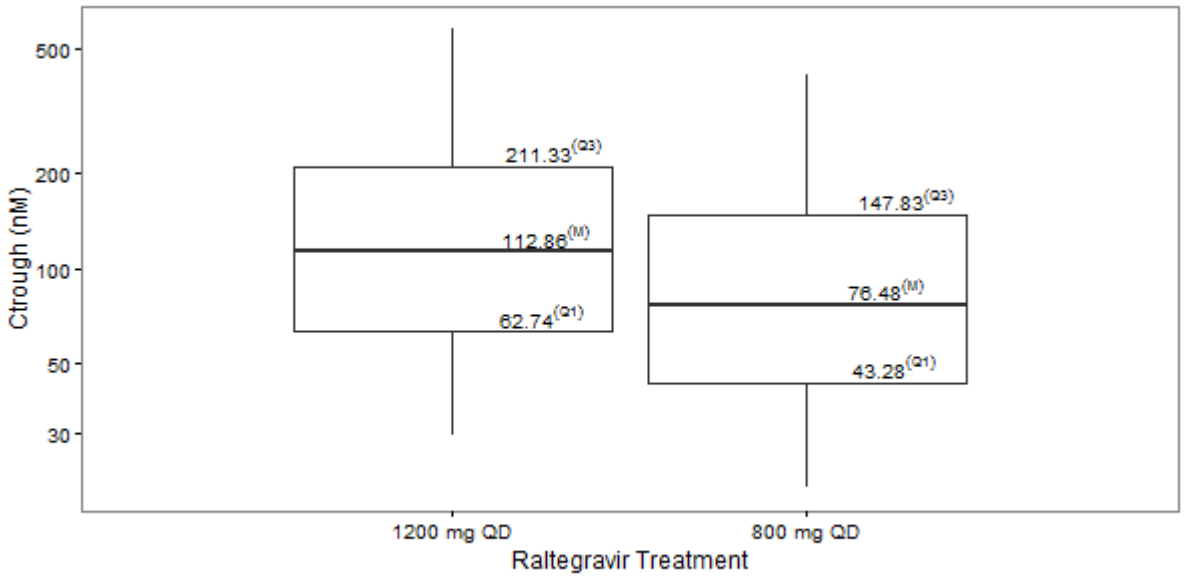
Efficacy:

PK/PD analyses for raltegravir and for other classes of HIV therapy indicate that C_{trough} (i.e. C_{24hr} for raltegravir QD) is an appropriate PK parameter to characterize the clinical significance of reductions in raltegravir plasma concentrations on efficacy. In PN071 (QDMRK), raltegravir 800 mg QD (given as 2 x 400 mg tablets) failed to demonstrate non-inferiority to raltegravir 400 mg BID. Thus, to maintain non-inferior efficacy, it was considered necessary for the mean C_{trough} of raltegravir 1200 mg QD to exceed that observed with 800 mg QD from PN071. This superior PK was confirmed by results from PN292 and is illustrated in [Figure 2.7.2: 2], which shows higher raltegravir C_{trough} values from 1200 mg QD relative to 800 mg QD in PN071 in both central tendency and overall distribution. PK/PD analysis from PN071 demonstrated that a C_{trough} of 45 nM was the cutoff below which a greater risk of treatment failure was observed. This value corresponds closely to the 25^{th} percentile of the distribution of C_{trough} values (43.28 nM) with raltegravir 800 mg QD, and was well below the 25^{th} percentile value (62.74 nM) with raltegravir 1200 mg QD.

Thus, the lower bound of a clinically meaningful change in C_{trough} for 1200 mg QD must be greater than the ratio of raltegravir C_{trough} values observed from 800 mg QD in PN071 (median of 76.48 nM) and 1200 mg QD in PN292 (112.86 nM), which is 0.68. Since raltegravir 800 mg QD in PN071 had a very narrow miss (difference -5.7% [95% CI -10.7% to 0.83%] of 0.7% to the 10% non-inferiority margin, the lower bound was defined to be slightly above 0.68, at a value of 0.75. This corresponds to a raltegravir C_{trough} value of 84.6 nM based on the median C_{trough} observed from 1200 mg QD, which is well above the 45 nM cutoff associated with greater treatment failure and the median C_{trough} from raltegravir 800 mg QD in PN071 (76.48 nM). In conclusion, it is proposed that no clinically relevant difference in the efficacy of raltegravir 1200 mg QD is anticipated for factors that decrease raltegravir C_{trough} by <25%, specifically, the lower bound of the 90% confidence interval (CI) of C_{trough} geometric mean ratio (GMR) must be >0.75.

Figure 2.7.2: 2

Raltegravir C_{trough} Values from PN071 (800 mg QD) and PN292 (1200 mg QD)



Q1=25% Percentile, M=Median, Q3=75% Percentile, Whiskers=5% and 95% Percentiles

Data Source: [Ref. 5.3.5.3: 04C3B0]

Safety:

In general, AUC or C_{max} are the PK parameters most likely to be associated with toxicity. Prior experience with ISENTRESS® 400 mg BID has demonstrated that AUC is an appropriate raltegravir PK parameter to characterize the clinical significance of elevations in raltegravir plasma concentrations on safety. The daily raltegravir AUC values obtained with 1200 mg QD in PN292 are the highest attained in any long-term raltegravir clinical study to date. Since results from the safety analysis based on PK exposure quartiles demonstrated no increased risks associated with the highest quartile of the raltegravir exposures, the 95th

percentile of the entire distirubtion of steady-state AUC_{0-24} values from PN292 was determined as an appropriate exposure threshold for safety in adults, and was quantified as 109 µM*h [Ref. 5.3.5.3: 04C3B7]. Therefore, the upper bound of a clinically meaningful change could be defined by this high exposure subpopulation from PN292 with an acceptable safety profile. This would provide a ratio of close to 2 relative to the median of AUC_{0-24} (54.6 µM*h). In PN293, a 28-day placebo-controlled study with 1800 mg raltegravir, no subjects experienced ALT >5x ULN in the study. One subject experienced ALT >3x ULN and one subject experienced ALT >2x ULN. Modest elevations in GGT, never exceeding 2 x ULN, were observed in these subjects. Alkaline phosphatase, total and direct bilirubin levels were all within normal limits throughout the dosing period. These changes were not considered clinically meaningful, supported by the lack of clinically significant symptoms and observed improvements while on treatment. No subjects were discontinued because of these changes. The pharmacokinetic exposures at 1800 mg raltegravir QD were modestly higher than at 1200 mg QD. There were no apparent relationship with raltegravir PK exposure. These changes were not considered clinically significant because of a lack of clinically significant symptoms, and observed improvements while on treatment. In conclusion, based only on exposure/safety analysis from PN292 which provides a large dataset, it is proposed that no clinically relevant difference in the safety of raltegravir 1200 mg QD is anticipated for factors that increase raltegravir AUC_{0-24} by <100%, specifically, the upper bound of the 90% CI of AUC_{0-24} GMR must be <2.00.

2 SUMMARY OF RESULTS OF INDIVIDUAL STUDIES AND INTEGRATED MODELING ANALYSIS

2.1 Summary of Results of Individual Studies

This section provides a brief summary of the four Phase 1 clinical pharmacology studies (PN293, PN812, PN823 and PN824) that were conducted as part of the raltegravir Once Daily Development Program. For the Phase 1 biopharmaceutic studies, refer to [Sec. 2.7.1].

2.1.1 Summary of Human Pharmacokinetic Studies

Four (4) Phase 1 studies were conducted to evaluate the clinical pharmacology of raltegravir 1200 mg QD (2 x 600 mg tablets) in healthy and HIV infected subjects and included a multiple dose pharmacokinetic study (PN293), an efavirenz interaction study (PN812), an atazanavir interaction study (PN823) and an antacid interaction study (PN824). A tabular summary of the PK and safety results from each study are provided in [Appendix 2.7.2: 1]. A narrative summary of the PK results from each study is provided below.

2.1.1.1 Multiple-Dose Pharmacokinetics of Raltegravir Once Daily in Healthy Subjects (PN293)

This study was a double-blind, randomized, placebo-controlled, multiple-dose study in 24 (N=18 active, N=6 placebo) healthy, adult male and female subjects to evaluate the safety and pharmacokinetics of raltegravir 1800 mg QD (3 x 600 mg tablets for once daily use) administered for 28 days. Blood samples were collected throughout the treatment period up to 24 hours following the last dose administration of study drug on Day 28.

Pharmacokinetics: The pharmacokinetics were comparable after 14 and 28 days of administration of raltegravir 1800 mg QD (3 x 600 mg). The mean values of C_{max}, C_{24hr}, AUC_{0-24hr} were 25.3 µM, 110 nM, 60.3 µM.h, and 29 µM, 88.5 nM, 74.5 µM.h after multiple-dose administration of raltegravir on Days 14 and 28, respectively. The median value of T_{max} was 1.5 hours after multiple-dose administration of raltegravir on Days 14 and 28.

A summary of safety can be found in [Appendix 2.7.2: 1] and in [Sec. 2.7.2.3.4].

2.1.1.2 Efavirenz Interaction Study (PN812)

This study was an open-label, randomized, 2-period, fixed-sequence study in 21 healthy, adult subjects. On Day 1 of Period 1, subjects received a single oral dose of raltegravir 1200 mg (2 x 600 mg tablets) in the evening followed by pharmacokinetic sampling up to 72 hours postdose. In Period 2, subjects received multiple oral doses of efavirenz 600 mg once daily for 14 consecutive days. A single oral dose of raltegravir 1200 mg (2 x 600 mg tablets) was coadministered with efavirenz on Day 12. Blood samples were collected up to 72 hours following raltegravir dosing on Day 12.

Pharmacokinetics: Raltegravir was rapidly absorbed with an observed median T_{max} of 1.5 hours following both treatments. The geometric mean apparent terminal $t_{½}$ values were similar following raltegravir alone and raltegravir + efavirenz (8.95 hours and 8.87 hours, respectively). Coadministration with efavirenz yielded GMRs (raltegravir + efavirenz/raltegravir alone) (90% CIs) for raltegravir $AUC_{0-\infty}$, C_{max}, and C_{24} of 0.86 (0.73, 1.01), 0.91 (0.70, 1.17), and 0.94 (0.76, 1.17), respectively. While the coadministration of efavirenz and raltegravir modestly reduces plasma levels of raltegravir, these changes are not considered to be clinically meaningful.

A summary of safety can be found in [Appendix 2.7.2: 1] and in [Sec. 2.7.2.3.4].

2.1.1.3 Atazanavir Interaction Study (PN823)

This study was an open-label, 2-period, fixed-sequence study in 14 healthy adult subjects under fed conditions. On Day 1 of Period 1, subjects received a single oral dose of raltegravir 1200 mg (2 x 600 mg tablets) followed by pharmacokinetic sampling for up to 72 hours postdose. In Period 2, multiple oral doses of atazanavir 400 mg were administered once daily for 9 consecutive days with a single oral dose of raltegravir 1200 mg (2 x 600 mg tablets) coadministered on Day 7. Blood samples were collected for 72 hours following raltegravir dosing on Day 7.

Pharmacokinetics: Coadministration with atazanavir yielded GMRs (90% CIs) for raltegravir $AUC_{0-\infty}$, C_{max}, and C_{24} of 1.67 (1.34, 2.10), 1.16 (1.01, 1.33), and 1.26 (1.08, 1.46), respectively. Since the upper bounds of the 90% CIs for the true GMRs were more than 1.25, a protocol pre-specified criteria, the primary hypothesis that the plasma $AUC_{0-\infty}$ and C_{max} for raltegravir after a multiple-dose regimen of atazanavir were not substantially altered compared with administration of raltegravir alone was not supported. A more comprehensive dataset from the PN292 study allowed for a more robust delineation of the

upper bound. Because the upper 90% CI of the raltegravir $AUC_{0-\infty}$ GMR obtained in the presence of atazanavir exceeded the upper clinical bound (2.00), coadministration of atazanavir with raltegravir QD is not recommended.

A summary of safety can be found in [Appendix 2.7.2: 1] and in [Sec. 2.7.2.3.4].

2.1.1.4 Antacid Interaction Study (PN824)

This study was an open-label, fixed-sequence, 4-treatment study, in 20 HIV-infected subjects. After a pre-treatment phase of raltegravir 1200 mg (2 x 600 mg tablets) for 5 days, subjects received the following: 1) raltegravir 1200 mg alone (2 x 600 mg tablets); 2) 3 tablets of TUMS® Ultra Strength (US) 1000 and raltegravir 1200 mg (2 x 600 mg tablets) given concomitantly; 3) 20 mL MAALOX® substitute Maximum Strength (MS) or a generic substitute given 12 hours after administration of raltegravir 1200 mg (2 x 600 mg tablets); and 4) 3 tablets of TUMS® Ultra Strength (US) 1000 given 12 hours after administration of raltegravir 1200 mg (2 x 600 mg tablets) over the four treatment periods. Blood samples were collected for 24 hours following raltegravir dosing in each treatment period.

Pharmacokinetics:. Three (3) tablets of TUMS® Ultra Strength 1000 mg given concomitantly with 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.28 (0.24, 0.32), 0.26 (0.21, 0.32), and 0.52 (0.45, 0.61) respectively, compared to 1200 mg raltegravir alone. Twenty (20) mL MAALOX® MS (or generic equivalent) given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.86 (0.73, 1.03), 0.86 (0.65, 1.15), and 0.42 (0.34, 0.52) respectively, compared to 1200 mg raltegravir alone. Three (3) tablets of TUMS® Ultra Strength 1000 given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.90 (0.80, 1.03), 0.98 (0.81, 1.17), and 0.43 (0.36, 0.51) respectively, compared to 1200 mg raltegravir alone. The metal-cation antacids generated clinically meaningful reductions in the plasma trough levels of raltegravir. Based on these data, coadministration of aluminum/magnesium and calcium carbonate antacids (concomitantly or staggered by 12 hours) with raltegravir QD is not recommended.

A summary of safety can be found in [Appendix 2.7.2: 1] and in [Sec. 2.7.2.3.4].

2.2 Summary of Integrated Modeling Analysis

A population-based approach was applied to determine the typical pharmacokinetics of raltegravir and identify the clinically significant covariates and their associated effect in healthy subjects and HIV-infected subjects, for raltegravir 1200 mg QD (2 x 600 mg). Exposure-efficacy modeling was conducted to examine the PK/PD relationship of raltegravir in HIV-infected subjects using results from PN292. Additionally, exploratory safety analyses based on raltegravir PK exposure quartiles were conducted to confirm the lack of a PK-safety relationship. To support the use of raltegravir 1200 mg QD (2 x 600 mg) in the pediatric patient population, simulation of raltegravir exposures in various weight bands was conducted to determine an appropriate weight cutoff. Together, the integrated modeling analyses were used to further support the final clinical dose recommendation for raltegravir once daily (1200 mg, 2 x 600 mg), which was previously supported by viral dynamics

modeling in the optimization of Phase 3 dose selection. A summary of these analyses are presented in the following sections.

2.2.1 Population Pharmacokinetic Analysis of Raltegravir Based on Raltegravir Once Daily Studies

Population PK modeling was conducted using data from 2 Phase 1 studies (PN290 and PN291), 3 DDI studies (PN812, PN823, and PN824), and 1 double-blinded Phase 3 study (PN292) following single and multiple doses of raltegravir 1200 mg QD (2 x 600 mg) [Ref. 5.3.5.3: 04C39T]. The final analysis dataset included a total of 618 subjects (4,624 PK samples), of which 94 subjects (2,325 PK samples) were from Phase 1 studies. Twenty-two to 30 serial blood samples for the measurement of raltegravir were drawn from each subject in the Phase 1 studies. Approximately 5 blood samples were drawn from each subject in PN292 with at least 1 sample from each of the following time periods: 1 to 4 hours postdose, 24 hours postdose, and anytime postdose. The data collected provided an opportunity to characterize raltegravir 1200 mg QD population pharmacokinetics in HIV treatment-naïve patients and healthy volunteers, as well as to evaluate the impact of covariates including body weight, race, ethnicity, gender, HIV infection, food effect (low, moderate, high-fat meals), concomitant medications such as UGT modulators (inhibitor or inducer), TUMS®, TRUVADA™, proton-pump inhibitors (PPIs), and H2 blockers. PN292 prohibited the use of strong UGT1A1 inducers (e.g., rifampin), anti-retroviral therapies other than raltegravir and TRUVADA™ (e.g., efavirenz, atazanavir), as well as metal-cation antacids. As such, population PK analysis of the UGT inducer or inhibitor effect and that of metal-cation antacids were based on Phase 1 DDI data.

A 2-compartment model with sigmoid absorption, lag time for doses administered with meals, and linear elimination described the concentration-time profile of raltegravir. The absorption lag for doses administered with food was 11 minutes and the duration of the sigmoid input ranged from 0.48 hours to 3.15 hours depending on the type of meal. The typical absorption rate constant was 0.678 1/hours and the typical value of clearance (CL) for a white/Asian subject weighing 72.8 kg and not receiving any concomitant medication was 50.2 L/h. The typical values of volume of distribution for the central compartment (Vc) and peripheral compartment (Vp) were 27.9 L and 66.5 L, respectively, with an intercompartmental CL of 3.92 L/h. While intrinsic and extrinsic factors were able to explain some of the variability in the PK of raltegravir, the remaining inter-individual variability (IIV) in CL was moderate (39% coefficient of variation [CV]) and the remaining IIV in all other PK parameters was high (62%CV to 104%CV). Given the differing shapes observed in the individual concentration-time profiles of the Phase 1 data, this level of IIV is reasonable. This highly variable pattern of absorption also contributed to a moderate to high degree of residual variability (RV) for the Phase 1 (42%CV) and Phase 3 (62%CV) data. Both %SEM and eta-shrinkage associated with the parameter estimates were <30% suggesting that all population and individual PK parameters were estimated with good precision and reasonable robustness. A prediction-corrected visual predictive check (VPC) analysis was performed to evaluate the predictive performance of the final population PK model. The overall prediction-corrected VPC exhibited extremely good correspondence for the central tendency (observed and simulated medians), and a good correspondence between the observed and simulated 5th and 95th percentiles of the concentration-time profiles. Using the analysis

dataset and the final model, bootstrap analyses were also performed. 95% of the models minimized successfully, and all parameter estimates of the final model were within the 95% prediction intervals of the bootstrap parameter estimates. It was therefore concluded that the final population PK model successfully captured the PK characteristics and data from both heathy volunteers and HIV treatment-naïve patients.

Covariate analysis showed that coadministration of atazanavir, efavirenz and TUMS® investigated in clinical DDI studies (PN812, PN823 and PN824) were statistically significant covariates of raltegravir PK. Consistent with the food effect observed in PN290, different meal types had different effects on raltegravir PK. Details on these effects are described in [Sec. 2.7.1.3.2]. Of the extrinsic and intrinsic factors that were not evaluated in dedicated clinical studies, race and body weight were statistically significant covariates of raltegravir clearance, resulting in higher raltegravir exposure in subjects of black/other race compared to white/Asian race, and in subjects of low body weight compared to typical body weight. Coadministration of TRUVADA™ was also found to have a statistically significantly effect on raltegravir relative bioavailability. Gender, ethnicity, HIV infection and coadministration of PPIs and H2 blockers were not found to be statistically significant covariates influencing raltegravir exposure. Additional details are described in [Sec. 2.7.2.3.2] and [Sec. 2.7.2.3.3].

The clinical relevance of the statistically significant covariate effects was also evaluated, and limited to covariates without dedicated clinical studies, which included race and body weight. A dataset of 1,000 virtual subjects was generated via re-sampling of the PN292 patient data and the Bayesian parameter estimates from the final model. Exposures for each subject were calculated to determine the geometric mean ratio (GMR) and corresponding 90% CI for the statistically significant covariates. In general, all exposures from the simulated dataset were within the raltegravir exposure ranges observed in PN292, which are associated with robust efficacy and an acceptable safety profile, so while such covariate effects are statistically significant, they are not likely to be clinically meaningful.

2.2.2 Population Exposure-Response Analyses for Efficacy

Exposure-efficacy analysis was conducted to assess the relationship between PK and efficacy endpoints of raltegravir 1200 mg QD (2 x 600 mg) and ISENTRESS 400 mg BID from PN292, and to confirm its consistency with previous understanding of the raltegravir PK/PD relationship from ISENTRESS® 400 mg BID [Ref. 5.3.5.3: 04C3B0]. The analyses included PK and treatment Week 48 efficacy data in PN292 (N=797 treatment naïve HIV patients), from both raltegravir 1200 mg QD (N=531) and ISENTRESS® 400 mg BID (N=266). Using observed sparse concentrations from both treatment arms, PK endpoints were determined and included C_{all_obs} (geometric mean of all observed concentrations for individual patient), C_{24_obs} (geometric mean of the observed concentration between 22 and 26 hours post-dose for 1200 mg QD), and C_{12_obs} (geometric mean of the observed concentration between 11 and 13 hours post-dose for 400 mg BID). Additionally, the population PK model developed for raltegravir 1200 mg QD was used to predict the steady-state C_{trough} values at 24 hour post-dose (C_{24}) in subjects from the QD treatment arm. Efficacy endpoints included the primary and secondary endpoints from PN292, achieving HIV-1 RNA <40 copies/mL and change from baseline in CD4 cell count, respectively. Logistic regression was conducted to examine the relationship between PK and HIV RNA <40 copies/mL, with screening viral

load (≤100,000 or >100,000 copies/mL), baseline CD4 cell count, and hepatitis B and/or C co-infection included for covariate evaluation. Additionally, the percent of patients achieving the viral suppression target (HIV-1 RNA <40 copies/mL) was also evaluated by quartiles of the PK endpoints. For the change from baseline in CD4 cell count, Pearson's correlation and Spearman's rank correlation with PK were calculated. Overall, findings from this analysis showed that for both raltegravir 1200 mg QD and ISENTRESS® 400 mg BID, maximum viral suppression (HIV-1 RNA <40 copies/mL) was likely achieved at the PK exposure range obtained with these treatment regimens in PN292. This is consistent with previous raltegravir PK/PD findings, which demonstrated that raltegravir data from ISENTRESS 400 mg BID is at the plateau region of the exposure-efficacy curve. Details of the results are described in [Sec. 2.7.2.1.3.2].

2.2.3 Population Exposure-Response Analyses for Safety

The raltegravir 1200 mg QD (2 x 600 mg) dosing regimen resulted in the highest exposure level observed in adults in a long-term study. Plasma exposure plateaued at 1200 mg and further increase in dose did not result in higher exposure, as observed in a Phase 1 study (PN293), where raltegravir 1800 mg QD (3 x 600 mg) exhibited similar exposures to those seen at a 1200 mg dose. Thus, the Phase 3 study PN292 provided the primary data to justify safety of raltegravir 1200 mg QD.

No clinically meaningful adverse events that were related to raltegravir administration were observed in PN292. Exploratory safety analyses based on PK exposure quartiles were conducted with data obtained from PN292 study. Steady state raltegravir PK exposure values were predicted for PN292 subjects using individual dosing, demographic information, and the most frequently occurring meal type for each subject throughout the study. Prior experience with raltegravir 400 mg BID indicates that AUC is the most appropriate PK parameter to characterize the clinical significance of elevations in raltegravir plasma concentrations on safety. Thus, the 95th percentile of the steady state PN292 $AUC_{0\text{-}24}$ exposure values was determined as an appropriate exposure threshold for safety in adults, and was quantified as 109 μM*h [Ref. 5.3.5.3: 04C3B7].

2.2.4 Modeling and Simulation of Pediatric Exposures for Raltegravir Once Daily

Raltegravir is approved for use as a BID regimen in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients as a 400 mg film-coated tablet (pediatric patients weighing at least 25 kg), and as weight-based dosing of a pediatric chewable tablet formulation in 100 mg (scored) and 25 mg strengths (≥ 11 kg), and a pediatric oral suspension formulation in 100 mg sachets (≥ 3 kg to < 20 kg). Simulation was conducted to define a weight cutoff that will support the use of 1200 mg QD (2 x 600 mg) in pediatric patients [Ref. 5.3.5.3: 04C3B7]. The goal was to predict pediatric exposures as a function of weight, and to find a weight range such that raltegravir exposures were contained within the exposure range determined to be safe in adults from PN292. Since the PK exposure in children is expected to be similar to or higher than adults following the administration of the same dosing regimen, efficacy in children is expected to be maintained, and safety is the primary focus of the pediatric exposure simulations.

The population PK model developed based on data from five Phase 1 studies (PN290, PN291, PN812, PN823, and PN824) and one Phase 3 study (PN292) in adults with a fixed allometric scaling approach was used to simulate steady state exposures in HIV-infected pediatric patients following administration of raltegravir 1200 mg QD. Previously, allometric scaling was shown to be a reasonable approach to extrapolate adult PK to children, particularly in pediatric population ≥ 6 months of age, when UGT1A1 (primary route of elimination) expression has reached adults levels. Additionally, both raltegravir apparent CL and V were shown to follow reasonably well with allometric scaling, assuming body weight to the power of 0.75 and 1 for clearance (CL) and volume (V), respectively [Ref. 5.3.3.5: 03RSDZ].

A virtual population of 1000 pediatric patients (10 weight groups in increments of 5 kg, 100 subjects per weight group) was generated based on the covariate data from the HIV-infected pediatric patients from the IMPAACT P1066/Merck PN022 study. Based on the pediatric dosing recommendations for 400 mg BID, the lowest weight included in this analysis was 25 kg. Enrichment of PN022 covariate data was applied to achieve a balanced and more robust sample size for the various weight groups, and was achieved by quantifying age and body weight relationships based on PN022 data. Steady state systemic exposures ($AUC_{0\text{-}24,ss}$, $C_{max,ss}$) were simulated as a function of weight, and for different subgroups to capture clinically relevant scenarios where raltegravir exposure may be increased, such as food effect (high-fat meal results a slight increase in raltegravir AUC relative to fasted condition), race (black/others had higher exposure than white/Asians in adults), and TRUVADA™ (coadministration resulted in higher exposure). In adults, the 95th percentile of the $AUC_{0\text{-}24,ss}$ exposure values from PN292 was determined as an appropriate safety exposure threshold, thus the weight cutoff in the pediatric population was identified at which the median of the $AUC_{0\text{-}24,ss}$ geometric means of the associated pediatric weight group is equal to or less than the adult safety exposure threshold. Results of the pediatric simulations showed that among the various subgroups evaluated, a weight cutoff of 40 kg appears to be adequate to achieve a safe administration of raltegravir 1200 mg QD while maintaining clinical efficacy [Sec. 2.7.2.3.2.2.1].

2.2.5 Viral Dynamics Modeling to Characterize Exposure-Response for Efficacy and to Optimize Once Daily Dose Selection for Raltegravir

To more fully characterize the exposure-response relationship for raltegravir efficacy and to predict the implications of changes in the pharmacokinetic profile on the efficacy of raltegravir, a PK/PD viral dynamics model was developed linking drug concentrations to viral inhibition, which in turn can be linked to treatment outcomes (e.g., decline in HIV viral load, % of patients with HIV RNA <50 copies/mL at a given timepoint). The general development of the model has been described in detail in a viral dynamics M&S report [Ref. 5.3.4.2: 03RLCB], while application of this model to project efficacy for 1200 mg QD and explore the likely impact of the food effect observed in PN291 is described in a separate report [Ref. 5.3.5.3: 04CNKQ].

The basic structure of the PK/PD viral dynamics model is based on the published model by Funk, et al. [Ref. 5.4: 03TTQ5] with the development of the model and parameter fits primarily driven by clinical data of short term monotherapy data from the raltegravir PN004

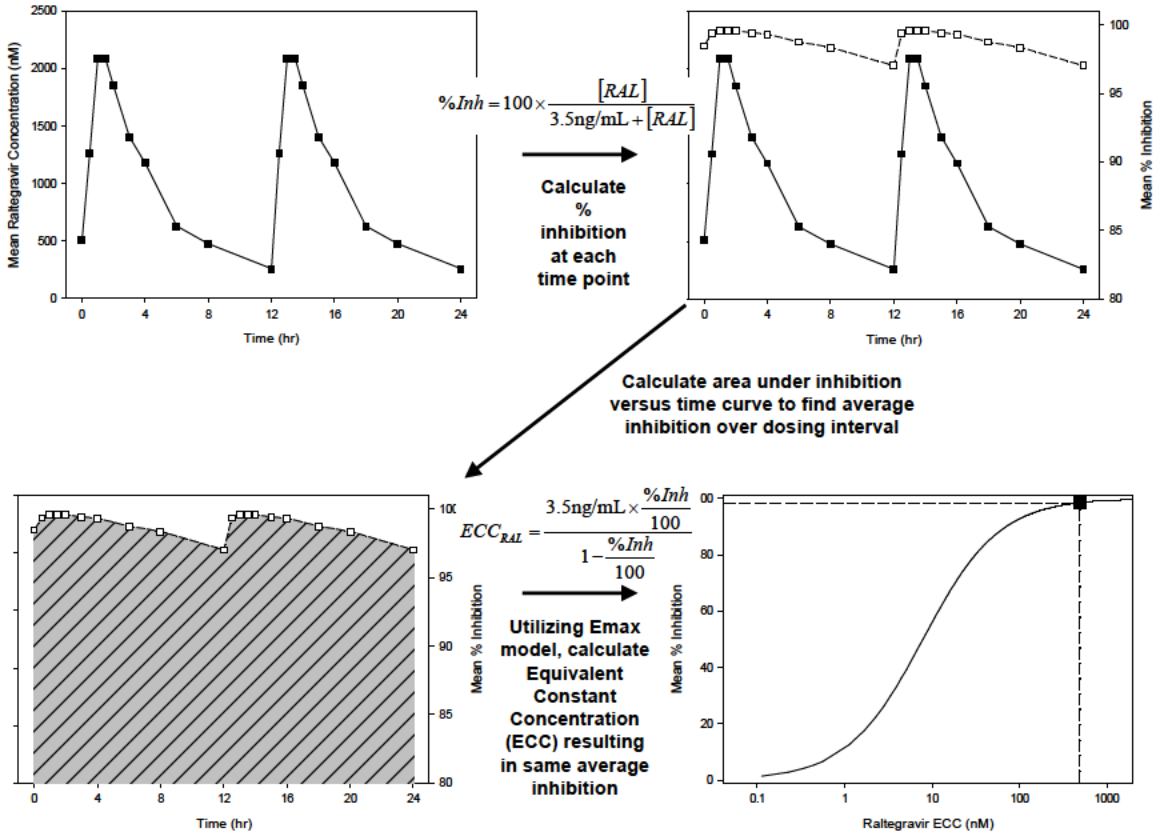
study and dolutegravir [Ref. 5.4: 03RL3R], along with long term combination therapy data from the raltegravir QDMRK study (PN071).

In this compartmental PK/PD viral dynamics model, target cells (uninfected CD4+ cells) are infected by the virus, leading to the production of actively infected cells, latently infected cells, or long-lived infected cells. Actively and long-lived infected cells generate virus, and latently infected cells are activated to become actively infected cells. The effect of integrase strand transfer inhibitors (InSTIs) and nucleoside revers transcriptase inhibitors (NRTIs) is to inhibit the infection of the target cells by the virus. Additionally, InSTIs contribute to the inhibition of the conversion rate from latently infected to actively infected CD4+ cells. An E_{max} model is used to describe the dependence of inhibition on drug exposure, with an in vivo EC_{50} values (raltegravir concentration resulting in 50% inhibition of infectivity and cell activation; with separate EC_{50} values for each) estimated for raltegravir from PN071 data. Resistant virus strains are included in the model, with resistance to each drug class characterized by an EC_{50} multiplier (resistance step size).

The PK/PD viral dynamics model incorporates information about the entire concentration-time profile of raltegravir. Using the entire shape of the profile is relevant as it was seen that C_{trough} but not daily AUC was predictive of efficacy in PN071. Using an E_{max} model (equation shown in [Figure 2.7.2: 3]) incorporating an in vivo EC_{50}, the raltegravir concentration versus time profile is converted to a profile of percent viral inhibition versus time with a calculated average inhibition over the dosing interval. From this average inhibition, again using the E_{max} model, a concentration can be calculated which would result in this same level of average inhibition over the dosing interval as if the concentration were held constant over the interval. This concentration is the Equivalent Constant Concentration, or ECC, and is the PK parameter which is used as the input in the viral dynamics model. [Figure 2.7.2: 3] below shows a schematic of the steps involved to translate the concentration versus time profile of raltegravir into the ECC value.

Figure 2.7.2: 3

Schematic of the Conversion of the Raltegravir Pharmacokinetic Profile into an Equivalent Constant Concentration (ECC) Value Utilizing a Sigmoidal Emax Model for Viral Inhibition (400mg BID Data Used as Example)

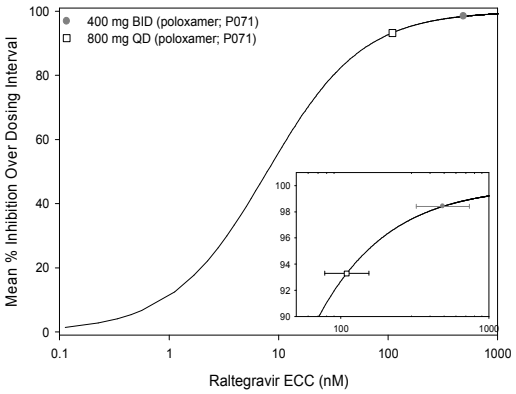


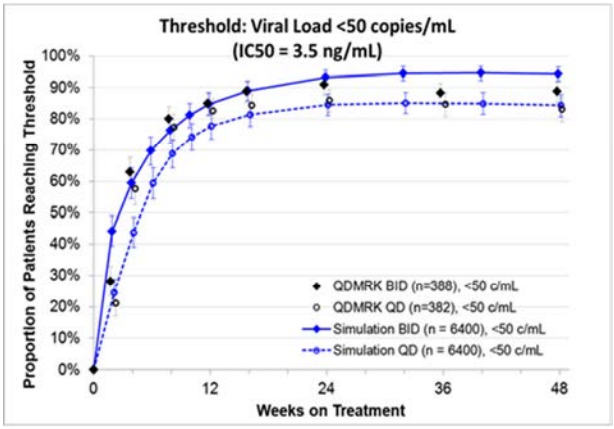
Data Source: [Ref. 5.3.5.3: 04CNKQ]

The in vivo EC_{50} values (raltegravir concentration resulting in 50% inhibition) for infectivity and cell activation were 3.5 ng/ml and 30 ng/ml, respectively, with simulation results being primarily driven by changes to the EC_{50} value associated with inhibition of infectivity. An EC_{50} value of 3.5 ng/mL or 8 nM on inhibition of infectivity was used for ECC calculations and found to best translate the differences in PK profiles between 800 mg QD and 400 mg BID regimens in adults into the observed difference in efficacy between these treatment arms. This model is able to correctly characterize the difference in efficacy observed in PN071 between the 400 mg BID and 800 mg QD raltegravir treatment arms based on the differences in PK profile observed for these dosing regimens [Figure 2.7.2: 4] while also adequately capturing the lack of dose-response observed in the BID dose ranging studies.

Figure 2.7.2: 4

Geometric Mean ECC and Percent Inhibition over the Dosing Interval for Patients Administered Raltegravir as 400 mg BID or 800 mg QD (left panel; inset: magnification of outer plot; error bars represent 95% confidence interval of ECC values) and Simulated Proportion of Adult HIV-Patients with Viral Loads <40 Copies/mL Over 48 Weeks (right panel)





Data Source: [Ref. 5.4: 03TSW9], [Ref. 5.3.4.2: 03RLCB]

In order to support selection of the QD dose and formulation for the Phase 3 study and to demonstrate that the raltegravir pharmacokinetic profiles associated with 1200 mg QD (2 x 600 mg) would be anticipated to result in efficacy similar to that obtained in adults with 400 mg BID, the full PK profiles from PN035 (a food effect study previously conducted for ISENTRESS® 400 mg BID in healthy subjects), PN290 and PN291 were used to calculate a distribution of steady state ECC values for each group, and the model was used to simulate the anticipated long-term efficacy for a combination regimen of raltegravir + NRTIs in treatment naïve HIV-infected patients with these PK profiles, with the results described in [Sec. 2.7.2.1.3]. In addition, the likely impact of the food effect observed in PN290 on efficacy was explored using this model, with the results described in [Sec. 2.7.1.3.2].

3 COMPARISON AND ANALYSES OF RESULTS ACROSS STUDIES

3.1 Pharmacokinetic Profile of Raltegravir Once Daily

Results from PN290, PN291, and PN293 demonstrate that raltegravir is rapidly absorbed with median time to maximum plasma concentration (T_{max}) ~1.5 to 2 hours in the fasted state. Relative to raltegravir 400 mg tablet, raltegravir 600 mg tablet formulation has higher dose-normalized systemic exposure (greater $AUC_{0\text{-}24hr}$/Dose by approximately 21-66%), and in general, a similar or smaller food effect. Administration of a low-fat meal appeared to decrease the rate and extent of absorption of 1200 mg QD raltegravir (on average, 42%

decrease in AUC, 52% decrease in C_{max}, and 16% decrease in C_{24hr}). Administration of a high-fat meal appeared to decrease the rate but not the extent of absorption of 1200 mg QD raltegravir (on average, 1.9% increase in AUC, 28% decrease in C_{max}, and 12% decrease in C_{24hr}). These effects are not expected to be clinically meaningful and raltegravir is administered with or without food in PN292, consistent with current labeling for raltegravir 400 mg BID [Sec. 2.7.1.3.2]. Once absorbed, raltegravir 1200 mg QD exhibits similar systemic pharmacokinetics to raltegravir 400 mg BID. The apparent terminal elimination half-life is approximately 9 to 12 hours with a shorter α-phase half-life (~1 hour) accounting for much of the AUC. Steady-state exposure is generally reached in 2 days, with little to no accumulation with multiple dose administration.

In PN292, sparse PK sampling was collected up to treatment Week 24, and was used to quantify raltegravir plasma concentration and to summarize the descriptive statistics of C_{all}, C_{trough}, and C_{min}. The geometric mean (GM) and corresponding 95% CI of C_{all}, C_{trough} and C_{min} after administration of multiple doses of 1200 mg QD were 963.52 nM (887.85, 1045.64) 122.08 nM (109.97, 135.53), and 79 nM (71.28, 87.54), respectively. The values of PK exposure endpoints, particularly C_{trough} and C_{min}, for raltegravir 400 mg BID observed in this study were generally consistent with those previously observed in the raltegravir twice daily development program. In an HIV-1 treatment-naïve patient population from PN824, the GM (95% CI) for steady state $AUC_{0\text{-}24hr}$ following 1200 mg QD raltegravir was 53.7 (44.2, 65.2) µM *hr, and for steady state C_{max} was 20.0 (16.5, 24.3) µM [Ref. 5.3.2.2: P824]. These values are consistent with the median values obtained from the population PK analysis of PN292, which were 54.6 µM *hr for $AUC_{0\text{-}24hr}$ and 16.9 µM for C_{max} [Ref. 5.3.5.3: 04C39T].

[Table 2.7.2: 1] provides a summary of PK data from PN292 for both treatment arms.

Table 2.7.2: 1

Summary Statistics for Raltegravir Sparse PK Parameters Following Administration of Multiple Oral Doses of Raltegravir 1200 mg QD and 400 mg BID to Treatment-Naïve HIV-Infected Patients From PN292

PK Exposure Endpoints	N	GM[†](95% CI)	% CV[‡]	Median	Min	Max
Raltegravir 1200 mg QD						
Call_obs (nM)	528	963.52 (887.85, 1045.64)	122.37	965.41	41.11	34476.32
C24_obs (nM)	389	122.08 (109.97, 135.53)	141.45	112.86	6.12	27048.81
Cmin (nM)	528	79.00 (71.28, 87.54)	179.93	73.81	4.88	17101.71
Raltegravir 400 mg BID						
Call_obs (nM)	261	851.19 (772.46, 937.95)	94.09	887.30	69.47	10414.61
C12_obs (nM)	148	557.25 (465.35, 667.30)	155.71	543.24	6.03	12128.71
Cmin (nM)	261	179.51 (155.63, 207.06)	171.51	192.62	5.85	7133.21

[†] Back-transformed from log scale.
[‡] % CV = 100 x sqrt(exp(s2) - 1), where s2 is the observed variance on the natural log-scale.
Min = Minimum. Max = Maximum. CI = Confidence Interval. CV = Coefficient of Variation.
Note: Raltegravir was administered with TRUVADA™
C24_obs: samples collected between 22 and 26 hours post-dose for the QD arm of the study
C12_obs: samples collected between 11-13 hours post-dose for the BID arm of the study
Cmin: minimum concentration value of all samples for an individual subject
Call_obs: all samples for an individual subject

Data source: [Ref. 5.3.5.1: P292V01]

3.2 Intrinsic Factors

This section provides an integrated summary of the effect of intrinsic factors on raltegravir PK. In general, effects of intrinsic factors on the exposure of raltegravir 1200 mg QD as evaluated in the population PK analysis [Ref. 5.3.5.3: 04C39T] were minimal to modest and were all within the exposure range observed for raltegravir from PN292 and the clinical significance bounds discussed in [Sec. 2.7.2.1.3.4]. As demonstrated in prior submission for ISENTRESS® 400 mg BID, moderate hepatic insufficiency and severe renal insufficiency had no clinically meaningful effect on raltegravir pharmacokinetics. Overall, the impact from the instrinsic factors evaluated are not clinically meaningful, and no specific clinical recommendations related to intrinsic factors are needed for raltegravir 1200 mg QD (2 x 600 mg) except for the pediatric dosing recommendation as described in [Sec. 2.7.2.3.2.2.1].

3.2.1 Body Weight

Population PK analysis showed that body weight had a statistically significant impact on apparent CL (CL/F); their relationship was described by a power model with CL/F increasing less than proportionally with increasing body weight. The median weight in the analysis dataset was 72.8 kg and has a typical CL value of 50.2 L/h ($AUC_{0\text{-}24hr}$ 54.9 uM*hr). For the lowest weight quartile (<63 kg), raltegravir exposure was increased, and the GMR (90% CI) relative to the reference weight group (middle two weight quartiles: 63 kg – 82.7 kg) for $AUC_{0\text{-}24}$ and C_{max} were 1.31 (1.25, 1.37), 1.15 (1.09, 1.22), respectively. Conversely, exposure decreased for the highest weight quartile (82.7 kg – 172 kg), thus the GMR (90% CI) for C_{trough} was 0.85 (0.77, 0.94). Overall, the impact of body weight on raltegravir exposure was within the variability observed from PN292 and the clinical bounds for efficacy and safety. No specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) with respect to body weight, with the exception of the pediatric dosing recommendation described in [Sec. 2.7.2.3.2.2.1].

3.2.2 Age

The impact of age on raltegravir 1200 mg QD PK was not specifically evaluated in a clinical study. However, previous population analysis of ISENTRESS® 400 mg BID concluded no significant impact on PK with respect to age, and consistent efficacy [Sec. 2.5.4.2.4.5] and safety [Sec. 2.5.5.3.1] were demonstrated in PN292 regardless of age. Therefore, no specific clinical recommendation for raltegravir is necessary. Administration of raltegravir 1200 mg QD (2 x 600 mg) in the pediatric population is recommended for patients weighing at least 40 kg; details are described in [Sec. 2.7.2.3.2.2.1].

3.2.2.1 Pediatric Use of Raltegravir Once Daily

Simulations using the population PK model developed for 1200 mg QD raltegravir and a body-weight based allometric scaling approach were conducted to support a pediatric dosing recommendation, with details described in [Sec. 2.7.2.2.2.4]. Results of the simulations showed that raltegravir exposure (steady state $AUC_{0\text{-}24}$) for pediatric patients with a body weight of 40 kg or higher are within the range of expsoures studied in adults in PN292. The highest simulated exposures were in black/other race pediatric patients receiving

TRUVADA™ both under fasted or high-fat meal conditions; in these two groups the simulated patients in the lowest acceptable weight group (≥40 and <45 kg) showed median exposures that are slightly above the predefined threshold, but the difference is small and the simulated expsoures for this group are still within the range observed in PN292 [Ref. 5.3.5.3: 04C3B7]. Given that all the pediatric simulated exposures were within the adult exposure range observed in PN292, and that there are no safety concerns at the same exposure values, a weight cutoff of 40 kg appears to be adequate to achieve a safe administration of raltegravir 1200 mg QD across all the evaluated subgroups while maintaining clinical efficacy.

3.2.3 Race/Ethnicity

In the population PK analysis, race was found to have a statistically significant impact on the apparent CL (CL/F). In subjects with race of Black or Other, CL/F was estimated to be lower by 18% relative to White and Asian subjects. With higher exposures in subjects of Black and Other racial background, the GMR (90% CI) relative to the White and Asian subjects for AUC_{0-24} and C_{max} were 1.31 (1.26, 1.37) and 1.15 (1.09, 1.21). Overall, the impact of race on raltegravir exposure was within the variability observed from PN292, and the exposure increase was well below the clinical bound for safety. This is also supported by efficacy and safety analyses from PN292, which demonstrated comparable response and tolerability across different racial groups [Sec. 2.5.4.2.4.5], [Sec. 2.5.5.3.1]. No specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) with respect to race.

Ethnicity (Hispanic vs non-Hispanic) was also evaluated in the population PK analysis and found to not impact raltegravir PK. Likewise, results from efficacy and safety analyses demonstrated comparable response and tolerability across different ethnicities [Sec. 2.5.4.2.4.5], [Sec. 2.5.5.3.1]. No specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) with respect to ethnicity.

3.2.4 Gender

Population PK analysis showed that gender was not a statistically significant covariate, and did not have an impact on raltegravir PK. This is consistent with findings from efficacy and safety analyses, which demonstrated comparable response and tolerability between males and females [Sec. 2.5.4.2.4.5], [Sec. 2.5.5.3.1]. No specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) dosing with respect to gender.

3.2.5 Renal Impairment

No renal impairment study was performed in the raltegravir Once Daily Development Program. Based on the renal impairment results described in previous raltegravir submissions, no specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) dosing.

3.2.6 Hepatic Impairment

No hepatic impairment study was performed in the raltegravir Once Daily Development program. Based on the hepatic impairment results described in previous raltegravir submissions, no specific clinical recommendation is needed for raltegravir 1200 mg QD (2 x 600 mg) dosing.

3.2.7 Disease

Population PK analysis showed that HIV infection was not a statistically significant covariate and did not have an impact on raltegravir PK. Results from efficacy and safety analyses also showed comparable response and tolerability between HIV viral subtypes (clade B vs. non-clade B) and baseline prognostic factors (HIV RNA levels and CD4 cell counts) [Sec. 2.5.4.2.4.5], [Sec. 2.5.5.3.1]. No specific clinical recommendation is needed for raltegravir 1200 mg (2 x 600 mg) dosing with respect to HIV infection.

3.3 Extrinsic Factors

This section provides an integrated discussion of the results from in vitro assessments, clinical studies evaluating DDIs and the population PK analysis as they pertain to the influence of extrinsic factors on raltegravir PK.

As described in [Sec. 2.7.2.1.1.1], the pharmacokinetic profiles are different for raltegravir 1200 mg QD and ISENTRESS® 400 mg BID (higher steady state daily AUC and C_{max} and lower C_{trough} for 1200 mg QD compared to 400 mg BID), therefore the criteria that define a clinically important change in PK are different, as described in [Sec. 2.7.2.1.3.4]. Evaluations of extrinsic factor effects for raltegravir 1200 mg QD were performed based on dedicated Phase 1 studies, population pharmacokinetic analysis, and evaluation of data from the previous raltegravir submissions in light of the clinical bounds for 1200 mg QD dosing. Based on the data from three DDI studies, a raltegravir/efavirenz interaction study in healthy volunteers (PN812), a raltegravir/atazanavir interaction study in healthy volunteers (PN823), and a raltegravir/antacid interaction study in HIV-infected subjects (PN824), coadministration of raltegravir 1200 mg QD with efavirenz is permitted; however, administration with atazanavir or aluminum/magnesium and calcium carbonate containing antacids (concomitantly or staggered by 12 hours) is not recommended. The impact of PPIs, H2 blockers or TRUVADA™ on raltegravir PK is not clinically meaningful as demonstrated by population PK analysis of raltegravir 1200 mg QD data from PN292. This is further supported by results from efficacy and safety analyses which showed that neither is affected by the use of PPIs and H2 blockers [Sec. 2.5.4.2.4.5], [Sec. 2.5.5.3.2]. Thus, coadministration of raltegravir 1200 mg QD with these agents is permitted. Additionally, the coadministration of raltegravir 1200 mg QD and strong inducers of drug metabolizing enzymes (e.g., rifampin, phenytoin and phenobarbital) or tipranavir/ritonavir is not recommended.

3.3.1 Drug-Drug Interactions

Overall, raltegravir has a low propensity to be involved in DDIs either as a victim or as a perpetrator. Findings from clinical studies conducted for ISENTRESS 400 mg BID to

evaluate the impact of raltegravir on coadministered drugs and to evaluate the impact on raltegravir PK by broad UGT1A1 inducers and inhibitors can be extended to raltegravir 1200 mg QD.

For raltegravir 1200 mg QD, specific clinical pharmacokinetic DDI studies were conducted with efavirenz, atazanavir, and aluminum/magnesium and calcium carbonate antacids to evaluate the effect of such coadministered drugs on raltegravir PK. Additionally, the impact of concomitant medications such as UGT modulators (inhibitor or inducer), TUMS®, TRUVADA™, PPIs and H2 blockers were also evaluated using combined Phase 1 and Phase 3 data and population PK analysis.

3.3.1.1 Effect of Raltegravir on Coadministered Drugs

Based on in vitro data [Sec. 2.7.2.1.2], raltegravir has a low propensity to be a perpetrator of DDIs at clinically relevant concentrations. In vitro, raltegravir does not inhibit or induce major drug metabolizing enzymes. In addition, raltegravir is not a potent inhibitor of drug efflux and uptake transporters in vitro. The potential for raltegravir to inhibit the renal uptake transporter OAT3 at maximal concentrations following 1200 mg QD (median C_{max} of 16.8 µM; unbound C_{max} of 2.8 µM) cannot be completely excluded based on in vitro data (IC_{50} of 18.8 µM); however, clinically meaningful DDI via this mechanism is unlikely, based on clinical drug interaction study results for raltegravir 400 mg BID with pravastatin [Ref. 5.4: 03RV3F] and tenofovir, known OAT3 substrates.

Findings from clinical DDI studies included in prior submissions demonstrated that raltegravir did not have a clinically meaningful effect on the pharmacokinetics of the following: hormonal contraceptives, methadone, tenofovir, midazolam, lamivudine, etravirine, darunavir/ritonavir and boceprevir. These conclusions made for raltegravir as a perpetrator can be extended to raltegravir 1200 mg once daily.

3.3.1.2 Effect of Coadministered Drugs on Raltegravir

Based on in vitro data, raltegravir is not a substrate of CYP enzymes and therefore, it is not expected to be a victim of DDIs via CYP inhibition or induction. Based on in vivo and in vitro studies, raltegravir is eliminated mainly by metabolism via a UGT1A1-mediated glucuronidation pathway and coadministration of UGT1A1 inhibitors or inducers may alter plasma levels of raltegravir.

Strong Inducers of Drug Metabolizing Enzymes:

The impact of rifampin (a strong inducer of drug metabolizing enzymes) on raltegravir 1200 mg QD is unknown, but co-administration is likely to decrease raltegravir trough levels based on the significant reduction in trough concentrations observed with raltegravir 400 mg BID; thus coadministration is not recommended. The impact of other strong inducers of drug metabolizing enzymes, such as phenytoin and phenobarbital, on UGT1A1 is unknown, therefore coadministration with raltegravir 1200 mg QD is not recommended.

Moderate and Weak Inducers of Drug Metabolizing Enzymes:

A drug interaction study (PN812) was conducted with efavirenz, a known moderate inducer of UGT1A1 (a primary elimination pathway for raltegravir), in order to assess whether decreases in raltegravir pharmacokinetics at a dose of 1200 mg (2 x 600 mg tablets) were clinically meaningful when coadministered with moderate inducers. Coadministration with efavirenz yielded GMRs (raltegravir + efavirenz/raltegravir alone) (90% CIs) for raltegravir $AUC_{0-\infty}$, C_{max}, and C_{24} of 0.86 (0.73, 1.01), 0.91 (0.70, 1.17), and 0.94 (0.76, 1.17), respectively [Ref. 5.3.2.2: P812]. In the population PK analysis, dosing with efavirenz was a significant covariate for raltegravir PK; however, the magnitude of effect was modest with a 15% decrease in raltegravir bioavailability [Ref. 5.3.5.3: 04C39T]. While the coadministration of efavirenz and raltegravir modestly reduces plasma levels of raltegravir, these changes are not considered to be clinically meaningful (lower bound of 90% CI of C_{24} GMR is greater than lower clinical bound of 0.75); therefore coadministration of efavirenz and other moderate and weak inducers is permitted with 1200 mg QD raltegravir.

Inhibitors of UGT1A1:

A drug interaction study (PN823) was conducted with atazanavir, a known inhibitor of UGT1A1. Atazanavir was selected to assess the expected upper limit of increases in raltegravir pharmacokinetics at a single dose of 1200 mg (2 x 600 mg tablets) anticipated due to inhibition of UGT1A1. Coadministration with atazanavir yielded GMRs (90% CIs) for raltegravir $AUC_{0-\infty}$, C_{max}, and C_{24} of 1.67 (1.34, 2.10), 1.16 (1.01, 1.33), and 1.26 (1.08, 1.46), respectively [Ref. 5.3.2.2: P823]. In the population PK model, coadministration of atazanavir decreased the absorption rate constant Ka by 25.2% and decreased apparent CL by 18.6% [Ref. 5.3.5.3: 04C39T]. The impact of atazanavir on raltegravir 1200 mg QD PK is significant, with an upper bound of 90% CI of AUC GMR greater than the upper clinical bound of 2.0; thus, coadministration of raltegravir 1200 mg QD and atazanavir is not recommended.

Metal-Cation Antacids:

A drug interaction study (PN824) was conducted with metal containing antacids in HIV-infected subjects. Based on data from the raltegravir 400 mg BID clinical development program, a study in HIV infected subjects was considered more clinically relevant than a healthy subject population. The binding of the metal-binding motif in raltegravir with the divalent metal cation contained in some antacids could result in decreased raltegravir absorption and diminished plasma concentrations at a dose of 1200 mg (2 x 600 mg tablets). Three (3) tablets of TUMS® Ultra Strength 1000 mg (calcium carbonate antacid) given concomitantly with 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.28 (0.24, 0.32), 0.26 (0.21, 0.32), and 0.52 (0.45, 0.61) respectively, compared to 1200 mg raltegravir alone. This is consistent with results from the covariate analysis from population PK modeling, which showed that coadministration of TUMS® decreased raltegravir bioavailability by 70% [Ref. 5.3.5.3: 04C39T]. Staggered dosing of calcium containing antacids was also examined, and also led to a decrase in raltegravir trough concentrations: three tablets of TUMS® Ultra Strength 1000 given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24},

Cmax, and C_{24} of 0.90 (0.80, 1.03), 0.98 (0.81, 1.17), and 0.43 (0.36, 0.51)] respectively, compared to 1200 mg raltegravir alone [Ref. 5.3.2.2: P824]. Twenty (20) mL MAALOX® MS (or generic equivalent; aluminium/magnesium hydroxide antacid) given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.86 (0.73, 1.03), 0.86 (0.65, 1.15), and 0.42 (0.34, 0.52) respectively, compared to 1200 mg raltegravir alone. Coadministration of raltegravir 1200 mg QD with metal-cation antacids generated clinically meaningful reductions in the plasma trough levels of raltegravir (lower bound of 90% CI of C_{24} GMR is lower than lower clinical bound of 0.75). Based on these findings, coadministration of aluminum/magnesium and calcium carbonate containing antacids (concomitantly or staggered by 12 hours) with raltegravir 1200 mg QD, is not recommened.

Proton-Pump Inhibitors (PPIs) and H2 Blockers:

Drugs that increase gastric pH, such as PPIs and H2 blockers, have been shown to increase raltegravir solubility, thus could potentially increase raltegravir systemic exposures. Previously, the impact of omeprazole on ISENTRESS® 400 mg BID was not found to be clinically significant, and the general use of PPIs and H2 blockers were permitted in PN292. Population PK analysis showed that PPIs or H2 blockers were not statistically significant covariates (decreased raltegravir relative bioavailability by 8.8%), which is consistent with the comparable efficacy and safety results obtained in the absence or presence of these gastric pH-altering agents [Sec. 2.5.4.2.4.5] and [Sec. 2.5.5.3.2]. Thus, coadministration of PPIs and H2 blockers and raltegravir 1200 mg QD is permitted.

Additional DDIs:

Previous studies of ISENTRESS® 400 mg BID showed that coadministration of tenofovir (a component of TRUVADA™) increased raltegravir exposure [Ref. 5.4: 03QMY6]. While TRUVADA™ was identified as a statistically significant predictor of raltegravir PK in the population PK model and increased raltegravir relative bioavailability by 12%, its impact is not clinically meaningful as all subjects in PN292 received TRUVADA™ as part of the study regimen, and no clinically significant adverse events were reported. Thus, coadministration of TRUVADA™ and raltegravir 1200 mg QD is permitted.

DDI studies from prior raltegravir submissions showed that ritonavir, tipranavir/ritonavir, boceprevir or etravirine did not have a clinically meaningful effect on the pharmacokinetics of raltegravir from ISENTRESS 400 mg BID, and no dose adjustments were needed. No data exist on these DDIs with raltegravir 1200 mg QD. While the magnitudes of change on raltegravir exposure from ISENTRESS 400 mg BID by ritonavir, boceprevir or etravirine were small, the impact from tipranavir/ritonavir was greater (GMR C_{trough}=0.45, GMR AUC=0.76). Therefore, coadministration of raltegravir 1200 mg QD and tipranavir/ritonavir is not recommended.

3.4 Summary of Safety Across Studies

A list of the treatment categories used and the corresponding sample size for each assigned treatment label category in the Phase 1 Pooled Safety Data (includes six Phase 1 studies

(PN290, PN291, PN293, PN812, PN823, PN824) is provided in [Table 2.7.2: 2]. For presentation of the pooled raltegravir Phase 1 adverse events, incidence data are reported in four treatment categories, as assigned in the safety database. The four treatment categories used for all the adverse event incidence tables and for the baseline demographics table are described in detail in [Table 2.7.2: 2] and include: raltegravir alone (shown as 'raltegravir'), raltegravir with other drugs (shown as 'raltegravir + other'), other drugs alone (shown as 'other') and placebo (shown as 'placebo'). The term "other drug" generally refers to a second drug given alone as part of a DDI study.

Due to the differing study designs of the Phase 1 studies, no statistical analysis for between-treatment testing was pre-specified for the pooled adverse event data.

Table 2.7.2: 2

Treatment Categories Used in the Phase 1 Pooled Safety Data (n=6 studies)

Treatment Categories	N per Assigned Therapy Labels
1: Raltegravir (MK-0518) Alone	**133**
Includes the following raltegravir doses given alone or in combination with placebo: single doses up to 1200 mg, and multiple doses of 1800 mg (3 x 600 mg) given once daily for up to 4 weeks (28 days).	
2: Raltegravir (MK-0518) with Other Drugs	**50**
Includes raltegravir doses given with atazanavir, efavirenz, and antacids.	
3: Other Drugs Alone	**35**
Includes the other drugs given alone (atazanavir, efavirenz, antacids).	
4: Placebo	**6**
Placebo	
This table includes subjects in crossover study designs, including DDI studies as well as studies where a different treatment could have been administered on different days of a given period; therefore a subject may be counted in more than one treatment category.	

Data Source: [Sec. 5.3.5.3.3]

The counts of all adverse events (≥5% incidence) by system organ class (SOC) for the 6 pooled Phase 1 studies are in [Table 2.7.2: 3]. The most commonly reported adverse events (those occurring at an incidence ≥5%) for raltegravir alone were headache (15%), hypertension (6.8%), myalgia (6%), and abdominal pain (5.3%), for raltegravir + other were diarrhea (6%) and upper respiratory tract infection (6%). Other presentations of the adverse events reported in Phase 1 studies are provided in [Sec. 5.3.5.3.3].

Table 2.7.2: 3

Subjects With Adverse Events (Incidence ≥ 5% in One or More Treatment Groups) Phase 1 Pooled Safety Data

	Raltegravir		Raltegravir + Other		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	133		50		35		6		119		139	
with one or more adverse events	64	(48.1)	17	(34.0)	27	(77.1)	6	(100.0)	4	(3.4)	96	(69.1)
with no adverse events	69	(51.9)	33	(66.0)	8	(22.9)	0	(0.0)	115	(96.6)	43	(30.9)
Blood and lymphatic system disorders	**1**	**(0.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(33.3)**	**0**	**(0.0)**	**3**	**(2.2)**
Eosinophilia	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Lymphadenitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Lymphadenopathy	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Cardiac disorders	**1**	**(0.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(16.7)**	**0**	**(0.0)**	**2**	**(1.4)**
Palpitations	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Eye disorders	**3**	**(2.3)**	**0**	**(0.0)**	**3**	**(8.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**6**	**(4.3)**
Gastrointestinal disorders	**23**	**(17.3)**	**4**	**(8.0)**	**7**	**(20.0)**	**4**	**(66.7)**	**0**	**(0.0)**	**35**	**(25.2)**
Abdominal pain	7	(5.3)	0	(0.0)	0	(0.0)	2	(33.3)	0	(0.0)	9	(6.5)
Aphthous stomatitis	1	(0.8)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	2	(1.4)
Diarrhoea	5	(3.8)	3	(6.0)	1	(2.9)	1	(16.7)	0	(0.0)	9	(6.5)
Nausea	6	(4.5)	0	(0.0)	3	(8.6)	3	(50.0)	0	(0.0)	12	(8.6)
General disorders and administration site conditions	**16**	**(12.0)**	**1**	**(2.0)**	**10**	**(28.6)**	**2**	**(33.3)**	**0**	**(0.0)**	**27**	**(19.4)**
Fatigue	6	(4.5)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	7	(5.0)
Feeling drunk	0	(0.0)	0	(0.0)	5	(14.3)	0	(0.0)	0	(0.0)	5	(3.6)
Feeling hot	1	(0.8)	0	(0.0)	5	(14.3)	1	(16.7)	0	(0.0)	6	(4.3)

Subjects With Adverse Events (Incidence ≥ 5% in One or More Treatment Groups)

	Raltegravir		Raltegravir + Other		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**16**	**(12.0)**	**1**	**(2.0)**	**10**	**(28.6)**	**2**	**(33.3)**	**0**	**(0.0)**	**27**	**(19.4)**
Instillation site irritation	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Infections and infestations	**9**	**(6.8)**	**4**	**(8.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**13**	**(9.4)**
Upper respiratory tract infection	4	(3.0)	3	(6.0)	0	(0.0)	0	(0.0)	0	(0.0)	7	(5.0)
Investigations	**9**	**(6.8)**	**1**	**(2.0)**	**1**	**(2.9)**	**0**	**(0.0)**	**3**	**(2.5)**	**14**	**(10.1)**
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(5.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**3**	**(2.2)**
Decreased appetite	0	(0.0)	0	(0.0)	2	(5.7)	1	(16.7)	0	(0.0)	3	(2.2)
Musculoskeletal and connective tissue disorders	**17**	**(12.8)**	**1**	**(2.0)**	**3**	**(8.6)**	**2**	**(33.3)**	**0**	**(0.0)**	**23**	**(16.5)**
Musculoskeletal pain	1	(0.8)	1	(2.0)	2	(5.7)	0	(0.0)	0	(0.0)	4	(2.9)
Musculoskeletal stiffness	5	(3.8)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	6	(4.3)
Myalgia	8	(6.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	9	(6.5)
Nervous system disorders	**28**	**(21.1)**	**3**	**(6.0)**	**21**	**(60.0)**	**4**	**(66.7)**	**1**	**(0.8)**	**52**	**(37.4)**
Dizziness	5	(3.8)	2	(4.0)	14	(40.0)	1	(16.7)	0	(0.0)	19	(13.7)
Dizziness postural	1	(0.8)	0	(0.0)	4	(11.4)	0	(0.0)	0	(0.0)	5	(3.6)
Headache	20	(15.0)	2	(4.0)	8	(22.9)	3	(50.0)	0	(0.0)	31	(22.3)
Sensory disturbance	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Somnolence	4	(3.0)	0	(0.0)	4	(11.4)	2	(33.3)	0	(0.0)	10	(7.2)

Subjects With Adverse Events (Incidence ≥ 5% in One or More Treatment Groups)

	Raltegravir		Raltegravir + Other		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**2**	**(1.5)**	**1**	**(2.0)**	**10**	**(28.6)**	**1**	**(16.7)**	**0**	**(0.0)**	**13**	**(9.4)**
Abnormal dreams	0	(0.0)	0	(0.0)	8	(22.9)	0	(0.0)	0	(0.0)	8	(5.8)
Insomnia	0	(0.0)	0	(0.0)	1	(2.9)	1	(16.7)	0	(0.0)	2	(1.4)
Respiratory, thoracic and mediastinal disorders	**12**	**(9.0)**	**0**	**(0.0)**	**2**	**(5.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**15**	**(10.8)**
Oropharyngeal pain	5	(3.8)	0	(0.0)	1	(2.9)	1	(16.7)	0	(0.0)	7	(5.0)
Skin and subcutaneous tissue disorders	**8**	**(6.0)**	**4**	**(8.0)**	**2**	**(5.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**13**	**(9.4)**
Pruritus	1	(0.8)	1	(2.0)	2	(5.7)	0	(0.0)	0	(0.0)	4	(2.9)
Skin sensitisation	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.7)
Vascular disorders	**10**	**(7.5)**	**1**	**(2.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**	**11**	**(7.9)**
Hypertension	9	(6.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)	9	(6.5)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Data Source: [Sec. 5.3.5.3.3]

Three subjects (2.2%) were discontinued from treatment due to non-serious adverse events after receiving raltegravir alone or in combination with other drugs. In general, the most common drug-related adverse events were headache, myalgia, and fatigue among subjects receiving raltegravir alone or in combination with other drugs. Most (96.5%) adverse events were generally transient and considered of mild intensity. There was 1 adverse event of severe blood creatine phosphokinase increased reported in a subject after receiving raltegravir 1200 mg QD alone. No deaths occurred in these studies. Overall, the adverse events that were reported are consistent with the known safety and tolerability profile of raltegravir. No clinically significant abnormalities were observed in routine blood and urine chemistry panels, completed blood count, electrocardiograms, physical examinations, and vital signs in any subject receiving either raltegravir alone, raltegravir with other drugs, other drugs alone or placebo in the Phase 1 studies. Safety finding from PN824 and PN293 are further described below.

PN824:

Four (4) serious adverse experiences (SAEs) were reported by 1 subject in PN824. This subject was briefly hospitalized for reported chest pain, dyspnoea, orthostatic hypotension and rash 9 days following dosing with raltegravir and TUMS® Ultra Strength (US) 12 hours later (Treatment D, Period 4). Upon arrival at the hospital, the subject noted the rash started after receiving raltegravir on Day -1 of Period 3, 2 days after receiving raltegravir with TUMS® Ultra Strength (US) (Treatment B, Period 2). Each of the SAEs were of moderate intensity. The rash was considered reasonably related to the study medication and resolved 21 days after it started. The chest pain, dyspnoea and orthostatic hypotension were considered not reasonably related to the study medication. The dysponea and chest pain resolved after approximately 2 weeks. The orthostatic hypotension resolved after 2 days. This subject was lost to follow up.

PN293:

In PN293, where subjects received 1800 mg raltegravir QD (3 x 600 mg tablets; N=18) or placebo (N=6), five subjects (293-02*, 03*, 04*, 05* and 06*; all on active) showed elevations in CPK. Among the five subjects, four (293-02*, 03*, 04* and 05*) did not show elevations until after the dosing had been completed and the subjects were no longer domiciled. Of the five subjects, two (293-03* and 04*) experienced CPK >20 x ULN and one (293-06*) experienced ~9 x ULN; for these three subjects, the intensity of the event was rated as severe by the investigator and was considered related to the study drug. One subject (293-02*) experienced >2 x ULN CPK increase and one other subject (293-05*) experienced <2 x ULN CPK increase. As described above, 293-02* showed a CPK level of 508 U/L two days post last dose (CPK values were within normal limits (WNL) throughout dosing period, i.e., <200 U/L). 293-03* showed a CPK level of 6070 U/L at the 2-week follow-up post study visit. 293-04* showed a CPK level of 4220 U/L, also at the 2-week follow-up post-study visit. 293-05* showed a CPK level of 359 U/L at the 2-week follow-up post-study visit. The LFT panels were WNL throughout the dosing period for 293-03*, 04* and 05*. 293-06* first had a CPK level elevation (1870 U/L) on Day 13 (described above). All subjects were closely monitored by the clinical site until values returned to normal range or stabilized.

No subjects experienced ALT >5x ULN in PN293. One subject (293-02*) experienced ALT >3x ULN and one subject (293-06*) experienced ALT >2x ULN, both were in the active treatment group. In the subject that experienced ALT >3x ULN, there were elevations in GGT (<2 x ULN) returning to within normal limits (WNL) by end of dosing period. CPK, alkaline phosphatase, total and direct bilirubin were all within WNL throughout the dosing period. Five subjects experienced ALT <2x ULN (293-07*, 08*, 09*, 10* and 11*). 293-08* and 10* received a placebo and 293-02*, 06*, 07*, 09* and 11* recieved 1800 mg raltegravir QD. These changes were not considered clinically significant because of a lack of clinically significant symptoms, and observed improvements while on treatment. There was no apparent relationship with raltegravir exposure. No subjects were discontinued because of these changes.

A thorough QTc study (PN024) was previously performed as part of the raltegravir twice daily development program and the data were included in a prior submission. PN024 was a double-blind, randomized, placebo-controlled, double-dummy, 3-period, balanced cross-over study in healthy volunteers evaluating a single oral dose of either 400-mg moxifloxacin, 1600-mg raltegravir (4 x 400 mg tablets), or placebo. The single supra-therapeutic 1600 mg dose of the raltegravir Phase 1 lactose formulation resulted in a C_{max} value of 19.6 μM and did not prolong the QTc interval. The upper limit of the 90% CI for the placebo-adjusted mean change-from-baseline of raltegravir was less than 10 msec at every time point (per the criteria set forth in ICH E14). Assay sensitivity was verified using the positive control (moxifloxacin). Enhanced ECG monitoring in PN293 at the 1800 mg dose showed no meaningful trends on QTc [Ref. 5.3.3.1: P293].

4 SPECIAL STUDIES

No special studies were conducted.

5 CONCLUSIONS

1. Following oral absorption, the systemic disposition of raltegravir 1200 mg QD (e.g., distribution and elimination kinetics) is comparable to that previously observed with ISENTRESS 400 mg BID. Raltegravir 1200 mg QD (2 x 600 mg tablets) has higher systemic exposure (greater AUC_{0-24} by approximately 21-66% compared to 1200 mg QD [3x400 mg tablets] and 2.3-fold compared to 400 mg BID). In Phase 1 studies in healthy adults and adults with HIV infection, both single doses of 1200 mg (administered as 2 x 600 mg tablets) and multiple doses of 1200 mg (administered as 2 x 600 mg tablets) or 1800 mg (administered as 3 x 600 mg tablets) QD were generally well tolerated. The safety profile of the 1200 mg QD regimen is consistent with prior findings in the BID program. The new dosing regimen is supported by the favorable safety profile of raltegravir QD.
2. Exposure-response relationships were characterized based on the results of the Phase 3 non-inferiority study PN292 of raltegravir 1200 mg QD vs. 400 mg BID which provided confirmatory evidence of the potent efficacy and the favorable safety profile of raltegravir 1200 mg QD (administered as 2 x 600 mg tablets).

a. Based on the efficacy analysis of PN292 by PK exposure quartiles (C_{trough} values), efficacy target in terms of viral suppression (HIV RNA < 40 copies/mL) was achieved even in the lowest quartile (< 25th percentile) of the C_{trough} values from raltegravir 1200 mg QD. No clinically significant association was found between PK exposures and the primary (HIV RNA < 40 copies/mL) and secondary efficacy (change in CD4 cell counts) endpoints for raltegravir QD and BID, and maximum response was likely achieved across the PK exposure range resulting from both QD and BID treatment regimens. Exposure-efficacy analysis of raltegravir supports that continued treatment with raltegravir 1200 mg QD is comparable to continued treatment with raltegravir 400 mg BID; thus, patients suppressed on raltegravir BID can be switched to raltegravir QD, with equivalent virologic outcomes.

b. No clinically meaningful adverse events that were related to raltegravir administration were observed in PN292. Exploratory safety analyses based on PK exposure quartiles (AUC_{0-24h} and C_{max}) confirmed the lack of any potential increased risks associated with the highest exposures from the raltegravir 1200 mg QD regimen.

3. No clinically relevant difference in the efficacy of raltegravir 1200 mg QD is anticipated for factors that decrease raltegravir Ctrough by <25%, specifically, the lower bound of the 90% confidence interval (CI) of C_{trough} geometric mean ratio (GMR) must be >0.75. Additionally, no clinically relevant difference in the safety of raltegravir 1200 mg QD is anticipated for factors that increase raltegravir AUC_{0-24} by <100%, specifically, the upper bound of the 90% CI of AUC_{0-24} GMR must be <2.00. Intrinsic and extrinsic factor effects that fall within these clinical comparability bounds are considered not clinically relevant and no alteration in the dosing guidance would be needed for those factors.
4. Raltegravir has a low propensity to be involved in DDIs either as a victim or as a perpetrator. Findings from clinical studies conducted for ISENTRESS 400 mg BID to evaluate the impact of raltegravir on coadministered drugs, and to evaluate the impact on raltegravir PK by coadministered drugs (e.g., strong inducers of drug metabolizing enzymes) can be extended to raltegravir 1200 mg QD. The impact of strong inducers of drug metabolizing enzymes (e.g., rifampin, phenytoin and phenobarbital), and tipranavir/ritonavir on raltegravir 1200 mg QD are unknown, but given their significant potential to decrease raltegravir trough levels, coadministration of these agents with raltegravir 1200 mg QD is not recommended.
5. DDIs between raltegravir 1200 mg QD and efavirenz, atazanavir or aluminum/ magnesium and calcium carbonate containing antacids (TUMS® and MAALOX®) were investigated in dedicated Phase I clinical studies. Interaction with efavirenz was not clinically meaningful, and coadministration of moderate and weak inducers with raltegravir 1200 mg QD is permitted. However, the impact of atazanavir and aluminum/magnesium and calcium carbonate antacids on raltegravir 1200 mg QD pharmacokinetics was significant and their coadministration is not recommended. Findings from population PK analysis demonstrated that raltegravir 1200 mg QD pharmacokinetics did not vary to a clinically meaningful extent with respect to coadministration with TRUVADA™, PPIs, and H2 blockers therefore coadministration of these agents with raltegravir 1200 mg QD is permitted.

6. Consistent with conclusions for ISENTRESS 400 mg BID, raltegravir 1200 mg QD pharmacokinetics in adults do not vary to a clinically meaningful extent with respect to body weight, gender, race, ethnicity, and HIV infection. As such, no specific clinical recommendation regarding these factors is needed for raltegravir 1200 mg (2 x 600 mg) dosing. Additionally, specific attributes of raltegravir pharmacokinetics from the raltegravir twice daily development program are considered applicable to the current Once Daily Development program, including renal impairment, hepatic impairment and effect on QTc.
7. Raltegravir 1200 mg QD has not been evaluated in a pediatric clinical study. However, simulations indicate that this dose and regimen can be recommended in pediatric patients with a body weight of at least 40 kg, and will result in raltegravir exposures within the range observed in adults in PN292.

6 APPENDIX

Appendix 2.7.2: 1

Clinical Pharmacology Studies Assessing PK in the Raltegravir Once Daily Development Program

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
Module 5.3.3.1 Healthy Subject PK and Initial Tolerability Studies								
P293	Evaluate the safety and pharmacokinetics of multiple doses raltegravir once-daily in healthy subjects.	22	2	20-54	Raltegravir 1800 mg (3x 600 mg tablets)	[redacted]	**Pharmacokinetic:** The pharmacokinetic (PK) parameters AUC0-24, Cmax, C24, and Tmax were estimated. **Safety:** Safety evaluations included clinical assessment of tolerability, physical examinations, semi-recumbent vital signs, 12-lead electrocardiogram, laboratory safety tests (chemistry, hematology, urinalysis), and evaluation of adverse experiences.	**Pharmacokinetic:** <u>Raltegravir 1800 mg dose as 3 x 600 mg QD for 28 days</u> ▪ Cmax, C24hr, AUC0-24hr were 25300 nM, 110 nM, 60300 h·nM and 29000 nM, 88.5 nM, 74500 h·nM after multiple administration of raltegravir on Days 14 and 28, respectively. ▪ The median value of Tmax was 1.5 hours after multiple administration of raltegravir on Days 14 and 28 in healthy subjects. ▪ It appears that the pharmacokinetics was comparable after multiple administration of raltegravir on Days 14 and 28 in healthy subjects. ▪ The percentage of subjects with trough concentrations of raltegravir >45 nM after multiple administration of raltegravir on Days 7, 10, 14, 21 and 28 ranged from 56 to 78%. **Safety:**
					Placebo to raltegravir 600 mg	[redacted]		

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								▪ The 1800 mg dose as 3 x 600 mg for 28 days was generally well-tolerated throughout the study. ▪ There were no serious clinical or laboratory adverse events reported during the treatment portion of the study and no subjects were discontinued from the study due to an adverse experience. ▪ A total of 160 adverse experiences (AE) were reported in 23 of 24 subjects, 127 AEs were reported in 17 subjects after administration of raltegravir 1800 mg and 33 AEs were reported in 6 subjects after administration of the matched placebo. In total, 23 subjects reported an AE that was considered related to the study drug by the investigator (17 subjects after 1800 mg raltegravir and 6 subjects after placebo). There were three (3) severe AEs of CPK elevations (described in more detail below) in the active treatment group. Adverse events reported by >3 subjects include headache (9 active, 3 placebo), dizziness (4 active, 1 placebo), myalgia (8 active, 1 placebo), back pain (4 active), musculoskeletal stiffness (4 active, 1 placebo), abdominal pain (6 active, 2 placebo), oropharyngeal pain (5 active, 1 placebo), fatigue (5 active, 1 placebo), nasopharyngitis (4 active), and pollakiuria (4 active).

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								▪ Seven subjects experienced elevations above the upper limit of normal range for ALT (ULN 45 U/L) and/or AST (ULN 40 U/L) while on treatment – 5 on active, and 2 on placebo. The elevations in ALT and AST were not associated with clinical symptoms and resolved or improved while on treatment. No subjects were discontinued and no subjects stopped or interrupted treatment because of these laboratory changes.. The elevations in AST/ALT did not exceed 5x ULN. ▪ Five subjects (all on active treatment) developed elevations in serum creatine phosphokinase (CPK). Of these, two subjects experienced CPK >20x ULN (ULN 200 U/L) and one subject experienced ~9x ULN CPK elevation. For these subjects, the CPK elevation was assessed as severe and considered related to the study drug. Out of the 5 subjects with CPK elevation, 4 subjects did not show elevations until after the dosing had been completed and the subjects were no longer domiciled. All subjects were closely monitored by the clinical site until values returned to normal range or stabilized. ▪ ECG and vital sign parameters were monitored throughout the study and no clinically meaningful changes from baseline values were observed.

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
Module 5.3.2.2 Hepatic Metabolism and Drug Interaction Studies								
PN812	Evaluate the effect of the coadministration of raltegravir and efavirenz on the pharmacokinetics of raltegravir once daily in healthy subjects	19	2	21-52	Raltegravir 1200 mg (2 x 600 mg tablets) 600 mg efavirenz	[redacted] Not Applicable	**Pharmacokinetic:** The pharmacokinetic (PK) parameters, AUC0-∞, Cmax, C24, Tmax, and apparent terminal t½ were estimated. **Safety:** Safety evaluations included clinical assessment of tolerability, physical examinations, semi-recumbent vital signs, 12-lead electrocardiogram, laboratory safety tests (chemistry, hematology, urinalysis), Columbia Suicide Severity Rating Scale (C-SSRS) questionnaire, and evaluation of adverse experiences.	**Pharmacokinetic:** <u>Raltegravir 1200 mg dose as 2 x 600 mg with and without 600 mg efavirenz</u> ▪ Raltegravir was rapidly absorbed with an observed median Tmax of 1.5 hours following both treatments. ▪ The geometric mean apparent terminal t½ values were similar following raltegravir alone and raltegravir + efavirenz (8.95 hours and 8.87 hours, respectively). ▪ Coadministration with efavirenz yielded GMRs (raltegravir + efavirenz/ raltegravir alone) (90% CIs) for raltegravir AUC0-∞, Cmax, and C24 of 0.86 (0.73, 1.01), 0.91 (0.70, 1.17), and 0.94 (0.76, 1.17), respectively. **Safety:** ▪ Administration of single 1200 mg oral doses of raltegravir alone and co-administered with multiple oral doses of efavirenz was generally well tolerated in healthy male and female subjects. ▪ There were no serious AEs (SAEs), events of clinical interest (ECIs), pregnancies, or deaths reported during the study.

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								▪ Twenty subjects reported treatment-emergent AEs (TEAEs), including 5 subjects following raltegravir alone, 20 subjects following efavirenz alone, and 5 subjects following raltegravir + efavirenz. The most commonly reported AEs in the study were dizziness, headache, and abnormal dreams. ▪ Twenty subjects reported drug-related AEs, including 3 subjects following raltegravir alone, 20 subjects following efavirenz alone, and 2 subjects following raltegravir + efavirenz. The most common drug-related AEs following efavirenz alone were dizziness and headache. ▪ One (1) subject discontinued from the study by the Investigator prior to the second dose of efavirenz alone due to the AEs of dizziness and feeling drunk. ▪ The majority of AEs were of mild intensity, transient, and resolved without interruption of treatment. Two (2) AEs were of moderate intensity. The majority of AEs were resolved by the end of the study with the following exceptions: mild blepharospasm and mild rash for 1 subject; and mild dysuria and mild scrotal pain for 1 subject. These 4 AEs were considered not related to study drug by the Investigator.

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								▪ There were no clinically meaningful treatment-related changes in laboratory, vital signs, C-SSRS, or ECG safety parameter values.
PN823	Evaluate the effect of the coadministration of raltegravir and atazanavir on the pharmacokinetics of raltegravir once daily in healthy subjects	5	9	21-55	Raltegravir 1200 mg (2 x 600 mg tablets) 400 mg atazanavir	[redacted] Not Applicable	**Pharmacokinetic:** The pharmacokinetic (PK) parameters, AUC0-∞, Cmax, C24, Tmax, and apparent terminal t½ were summarized. **Safety:** Safety evaluations included all types of adverse events (AEs), physical examinations, vital signs (heart rate and blood pressure), 12-lead electrocardiograms (ECGs), and clinical laboratory tests (hematology, serum chemistry, and urinalysis).	**Pharmacokinetic:** <u>Raltegravir 1200 mg dose as 2 x 600 mg with and without 400 mg atazanavir</u> ▪ Coadministration with atazanavir yielded GMRs (90% CIs) for raltegravir AUC0-∞, Cmax, and C24 of 1.67 (1.34, 2.10), 1.16 (1.01, 1.33), and 1.26 (1.08, 1.46), respectively. ▪ Since the upper bounds of the 90% CIs for the true GMRs were more than 1.25, the primary hypothesis that the plasma AUC0-∞ and Cmax for raltegravir after a multiple-dose regimen of atazanavir were not substantially altered compared with administration of raltegravir alone was not supported. **Safety:** ▪ Multiple oral doses of atazanavir and single oral doses of raltegravir were generally well tolerated when co-administered in healthy adult subjects in this study. ▪ No deaths, serious adverse events (SAEs), events of clinical interest

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								(ECIs), or pregnancies were reported during the study. ▪ The Investigator discontinued 1 subject on Day 5 of Period 2 due to the mild laboratory AEs of increased blood bilirubin and increased unconjugated blood bilirubin that were considered related to atazanavir alone. ▪ Ten (10, 71%) subjects reported AEs in this study, including 9 (65%) subjects who experienced AEs that were considered by the Investigator to be drug- related (1 subject each following raltegravir alone and raltegravir + atazanavir and 7 subjects following atazanavir alone). ▪ All AEs were of mild intensity and resolved by the end of the study. The most common drug-related AE reported in the study was nausea, which was reported by 3 (21%) subjects. ▪ There were no consistent treatment-related changes in laboratory, vital signs, or ECG safety parameter values.
PN824	Evaluate the effect of the coadministration of raltegravir and metal-cation antacids on the pharmacokinetics of	18	2	29-62	Raltegravir 1200 mg (2 x 600 mg tablets)	[redacted]	**Pharmacokinetic:** The pharmacokinetic (PK) parameters, AUC0-24, C24, Cmax and Tmax were calculated.	**Pharmacokinetic:** Raltegravir 1200 mg dose as 2 x 600 mg with and without TUMS® Ultra Strength 1000

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
	raltegravir once daily in HIV infected subjects				1000 mg TUMS®	5D126	**Safety:** Safety evaluations included assessments of adverse events, in addition to laboratory safety tests (hematology, serum chemistry and urinalysis), 12-lead electrocardiograms (ECGs) and vital signs.	▪ Steady state Cmax, AUC0-24 and C24 of raltegravir decreased by approximately 74%, 72% and 48%, respectively, when 1200 mg QD raltegravir is given concomitantly with 3 tablets of TUMS® Ultra Strength 1000. Median Tmax remained unchanged. ▪ Three (3) tablets of TUMS® Ultra Strength 1000 mg (calcium carbonate antacid) given concomitantly with 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.28 (0.24, 0.32), 0.26 (0.21, 0.32), and 0.52 (0.45, 0.61) respectively, compared to 1200 mg raltegravir alone. <u>MAALOX® MS (or generic equivalent) administered 12 hours after raltegravir 1200 mg dose as 2 x 600 mg</u> ▪ Steady state C_{max}, AUC_{0-24} and C_{24} of raltegravir decreased by approximately 14%, 14% and 58%, respectively, when 20 mL MAALOX® MS (or generic equivalent) is given 12 hours after administration of 1200 mg QD raltegravir. Median Tmax remained unchanged. ▪ Twenty (20) mL MAALOX® MS (or generic equivalent; aluminium/magnesium hydroxide
					20 mL MAALOX	5EK0517		

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								antacid) given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.86 (0.73, 1.03), 0.86 (0.65, 1.15), and 0.42 (0.34, 0.52) respectively, compared to 1200 mg raltegravir alone. <u>TUMS® Ultra Strength 1000 administered 12 hours after raltegravir 1200 mg dose as 2 x 600 mg</u> ▪ Steady state Cmax, AUC_{0-24} and C_{24} of raltegravir decreased by approximately 2%, 10% and 57%, respectively, when 3 tablets of TUMS® Ultra Strength 1000 is given 12 hours after administration of 1200 mg QD raltegravir. Median Tmax remained unchanged. ▪ Three (3) tablets of TUMS® Ultra Strength 1000 given 12 hours after administration of 1200 mg raltegravir yielded GMRs (90% CIs) for raltegravir AUC_{0-24}, C_{max}, and C_{24} of 0.90 (0.80, 1.03), 0.98 (0.81, 1.17), and 0.43 (0.36, 0.51)] respectively, compared to 1200 mg raltegravir alone. **Safety:** ▪ Raltegravir, administered alone or with TUMS® Ultra Strength (US) and MAALOX® MS (or generic equivalent), was generally well-

Study	Objectives/Design	Study Population			Dose (Dosage Forms)	Lot Number	Evaluation Criteria	Results
		M	F	Age Range				
Module 5.3.3 Human Pharmacokinetic Studies								
								tolerated in HIV-infected male and female subjects, at least 18 years of age. ▪ Most adverse experiences (AEs) reported were generally transient and considered mild to moderate intensity by the investigator. ▪ In total, 15 subjects (reported 37 AEs. The most frequently reported treatment emergent AEs were upper respiratory tract infection, diarrhoea and headache. Four (4) serious adverse experiences (SAEs) were reported by 1 subject in the study. This subject was briefly hospitalized for reported chest pain, dyspnoea, orthostatic hypotension and rash 9 days following dosing with raltegravir and TUMS® Ultra Strength (US) 12 hours later (Treatment D Period 4). Each of the SAEs were of moderate intensity. The rash was considered reasonably related to the study medication and resolved 21 days after it started. The chest pain, dyspnoea and orthostatic hypotension were considered not reasonably related to the study medication. The dyspnoea and chest pain resolved after approximately 2 weeks. The orthostatic hypotension resolved after 2 days. This subject was lost to follow up.

Data Source:[Ref. 5.3.2.2: P812, P823, P824] [Ref. 5.3.3.1: P293]

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

This Application proposes the licensure of a new dose strength and dosing schedule for raltegravir (once daily administration of raltegravir 1200 mg [2x600 mg] tablets). The efficacy of this new dose strength and dosing schedule was evaluated in a single study, Protocol 292, which is a Phase 3, multicenter, double-blind, randomized, active comparator-controlled clinical study that evaluated the safety and efficacy of raltegravir 1200 mg QD (2 x 600 mg tablets) versus raltegravir 400 mg BID, each in combination with TRUVADA™, in treatment-naïve HIV-1 infected subjects [Ref. 5.3.5.1: P292V01]. The primary efficacy endpoint of the study was to be measured at Treatment Week 48. Hence, this Application focuses on results of Protocol 292 through Treatment Week 48. The study will continue through Treatment Week 96.

This section provides an overview of the subject population and Treatment Week 48 efficacy data from Protocol 292. Because there is only one efficacy/safety study in support of this submission, and the summary of this information is included within the Module 2.5, clinical overview, the Applicant has focused this section on key efficacy tables that support the summary provided in Module 2.5 (see [Sec. 2.5.4]).

The enclosed tables describe findings through Treatment Week 48, with the exception of tables labeled “All Data Available”, which include data through 21-Dec-2015.

Table 2.7.3-qd1200: 1

Disposition of Subjects Not Randomized

	n (%)
Not Randomized	111
Lost To Follow-Up	2 (1.8)
Screen Failure	104 (93.7)
Subject Did Not Wish To Continue For Reasons Unrelated To Assigned Study Treatment	1 (0.9)
Withdrawal By Subject	4 (3.6)

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 2

Subjects Randomized by Investigator and Treatment Group

Location	Trial-Site	Investigator Name	Raltegravir 1200 mg QD (N=533)	Raltegravir 400 mg BID (N=269)	Total (N=802)
Argentina			**11**	**5**	**16**
Argentina	0518-292-		4	2	6
Argentina	0518-292-		4	2	6
Argentina	0518-292-		3	1	4
Australia			**16**	**14**	**30**
Australia	0518-292-		7	6	13
Australia	0518-292-		2	3	5
Australia	0518-292-		1	2	3
Australia	0518-292-		3	2	5
Australia	0518-292-		3	1	4
Belgium			**12**	**7**	**19**
Belgium	0518-292-		1	1	2
Belgium	0518-292-		8	4	12
Belgium	0518-292-		2	1	3
Belgium	0518-292-		1	1	2
Canada			**15**	**6**	**21**
Canada	0518-292-		4	2	6
Canada	0518-292-		1	0	1
Canada	0518-292-		4	2	6
Canada	0518-292-		2	1	3
Canada	0518-292-		1	0	1
Canada	0518-292-		3	1	4
Chile			**20**	**5**	**25**
Chile	0518-292-		7	2	9
Chile	0518-292-		8	1	9
Chile	0518-292-		2	1	3
Chile	0518-292-		3	1	4
Colombia			**16**	**3**	**19**
Colombia	0518-292-		6	3	9
Colombia	0518-292-		10	0	10
France			**22**	**13**	**35**
France	0518-292-		2	1	3
France	0518-292-		1	2	3
France	0518-292-		3	0	3
France	0518-292-		7	4	11
France	0518-292-		0	1	1

Subjects Randomized by Investigator and Treatment Group

Location	Trial-Site	Investigator Name	Raltegravir 1200 mg QD (N=533)	Raltegravir 400 mg BID (N=269)	Total (N=802)
France	0518-292-	[redacted]	3	1	4
France	0518-292-	[redacted]	1	2	3
France	0518-292-	[redacted]	5	2	7
Germany			**28**	**26**	**54**
Germany	0518-292-	[redacted]	1	2	3
Germany	0518-292-	[redacted]	1	2	3
Germany	0518-292-	[redacted]	3	3	6
Germany	0518-292-	[redacted]	2	2	4
Germany	0518-292-	[redacted]	1	3	4
Germany	0518-292-	[redacted]	4	1	5
Germany	0518-292-	[redacted]	6	2	8
Germany	0518-292-	[redacted]	5	5	10
Germany	0518-292-	[redacted]	0	1	1
Germany	0518-292-	[redacted]	5	5	10
Guatemala			**24**	**11**	**35**
Guatemala	0518-292-	[redacted]	10	6	16
Guatemala	0518-292-	[redacted]	9	1	10
Guatemala	0518-292-	[redacted]	3	2	5
Guatemala	0518-292-	[redacted]	2	2	4
Israel			**12**	**11**	**23**
Israel	0518-292-	[redacted]	4	0	4
Israel	0518-292-	[redacted]	1	0	1
Israel	0518-292-	[redacted]	2	5	7
Israel	0518-292-	[redacted]	2	3	5
Israel	0518-292-	[redacted]	3	3	6
Italy			**33**	**13**	**46**
Italy	0518-292-	[redacted]	4	1	5
Italy	0518-292-	[redacted]	3	2	5
Italy	0518-292-	[redacted]	6	3	9
Italy	0518-292-	[redacted]	5	0	5
Italy	0518-292-	[redacted]	6	2	8
Italy	0518-292-	[redacted]	4	2	6
Italy	0518-292-	[redacted]	2	2	4
Italy	0518-292-	[redacted]	3	1	4
Malaysia			**19**	**7**	**26**
Malaysia	0518-292-	[redacted]	5	1	6
Malaysia	0518-292-	[redacted]	4	3	7

Subjects Randomized by Investigator and Treatment Group

Location	Trial-Site	Investigator Name	Raltegravir 1200 mg QD (N=533)	Raltegravir 400 mg BID (N=269)	Total (N=802)
Malaysia	0518-292-		3	3	6
Malaysia	0518-292-		7	0	7
Peru			**6**	**2**	**8**
Peru	0518-292-		3	0	3
Peru	0518-292-		1	2	3
Peru	0518-292-		2	0	2
Philippines			**6**	**4**	**10**
Philippines	0518-292-		6	4	10
Portugal			**18**	**11**	**29**
Portugal	0518-292-		1	1	2
Portugal	0518-292-		1	4	5
Portugal	0518-292-		1	3	4
Portugal	0518-292-		8	2	10
Portugal	0518-292-		7	1	8
Russian Federation			**29**	**11**	**40**
Russian Federation	0518-292-		4	2	6
Russian Federation	0518-292-		8	2	10
Russian Federation	0518-292-		2	2	4
Russian Federation	0518-292-		3	1	4
Russian Federation	0518-292-		2	0	2
Russian Federation	0518-292-		1	1	2
Russian Federation	0518-292-		5	0	5
Russian Federation	0518-292-		4	3	7
South Africa			**43**	**14**	**57**
South Africa	0518-292-		6	0	6
South Africa	0518-292-		7	3	10
South Africa	0518-292-		19	8	27
South Africa	0518-292-		11	3	14
Spain			**24**	**14**	**38**
Spain	0518-292-		1	4	5
Spain	0518-292-		2	2	4
Spain	0518-292-		6	2	8
Spain	0518-292-		2	0	2
Spain	0518-292-		4	2	6
Spain	0518-292-		2	3	5
Spain	0518-292-		6	1	7

Subjects Randomized by Investigator and Treatment Group

Location	Trial-Site	Investigator Name	Raltegravir 1200 mg QD (N=533)	Raltegravir 400 mg BID (N=269)	Total (N=802)
Spain	0518-292-	[redacted]	1	0	1
Switzerland			**14**	**2**	**16**
Switzerland	0518-292-	[redacted]	4	0	4
Switzerland	0518-292-	[redacted]	3	2	5
Switzerland	0518-292-	[redacted]	5	0	5
Switzerland	0518-292-	[redacted]	2	0	2
Taiwan			**9**	**5**	**14**
Taiwan	0518-292-	[redacted]	2	1	3
Taiwan	0518-292-	[redacted]	3	2	5
Taiwan	0518-292-	[redacted]	4	2	6
Thailand			**36**	**16**	**52**
Thailand	0518-292-	[redacted]	5	0	5
Thailand	0518-292-	[redacted]	11	8	19
Thailand	0518-292-	[redacted]	7	2	9
Thailand	0518-292-	[redacted]	13	6	19
United Kingdom			**10**	**5**	**15**
United Kingdom	0518-292-	[redacted]	2	0	2
United Kingdom	0518-292-	[redacted]	4	1	5
United Kingdom	0518-292-	[redacted]	1	0	1
United Kingdom	0518-292-	[redacted]	0	1	1
United Kingdom	0518-292-	[redacted]	3	3	6
United States			**110**	**64**	**174**
United States	0518-292-	[redacted]	6	1	7
United States	0518-292-	[redacted]	2	0	2
United States	0518-292-	[redacted]	2	5	7
United States	0518-292-	[redacted]	7	2	9
United States	0518-292-	[redacted]	3	3	6
United States	0518-292-	[redacted]	1	2	3
United States	0518-292-	[redacted]	1	1	2
United States	0518-292-	[redacted]	4	4	8
United States	0518-292-	[redacted]	3	2	5
United States	0518-292-	[redacted]	3	5	8
United States	0518-292-	[redacted]	4	0	4
United States	0518-292-	[redacted]	3	0	3
United States	0518-292-	[redacted]	2	6	8
United States	0518-292-	[redacted]	2	0	2
United States	0518-292-	[redacted]	1	1	2
United States	0518-292-	[redacted]	6	4	10
United States	0518-292-	[redacted]	6	1	7

Subjects Randomized by Investigator and Treatment Group

Location	Trial-Site	Investigator Name	Raltegravir 1200 mg QD (N=533)	Raltegravir 400 mg BID (N=269)	Total (N=802)
United States	0518-292-	[redacted]	6	4	10
United States	0518-292-	[redacted]	6	2	8
United States	0518-292-	[redacted]	5	2	7
United States	0518-292-	[redacted]	3	3	6
United States	0518-292-	[redacted]	9	2	11
United States	0518-292-	[redacted]	3	0	3
United States	0518-292-	[redacted]	0	2	2
United States	0518-292-	[redacted]	2	2	4
United States	0518-292-	[redacted]	0	1	1
United States	0518-292-	[redacted]	7	1	8
United States	0518-292-	[redacted]	1	2	3
United States	0518-292-	[redacted]	1	1	2
United States	0518-292-	[redacted]	7	4	11
United States	0518-292-	[redacted]	4	1	5

N = Number of subjects randomized in the treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 3

Subject Status by Treatment Group
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Total Entered	533		269		802	
Not Treated	2	(0.4)	3	(1.1)	5	(0.6)
Treated	531	(99.6)	266	(98.9)	797	(99.4)
Discontinued Study	41	(7.7)	24	(8.9)	65	(8.1)
Adverse Event	6	(1.1)	6	(2.2)	12	(1.5)
Death	0	(0.0)	1	(0.4)	1	(0.1)
Lack Of Efficacy	4	(0.8)	1	(0.4)	5	(0.6)
Lost To Follow-Up	8	(1.5)	4	(1.5)	12	(1.5)
Non-Compliance With Study Drug	5	(0.9)	4	(1.5)	9	(1.1)
Physician Decision	4	(0.8)	0	(0.0)	4	(0.5)
Pregnancy	2	(0.4)	0	(0.0)	2	(0.2)
Withdrawal By Subject	12	(2.3)	8	(3.0)	20	(2.5)

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.
n (%)= Number (percent) of subjects in each sub-category.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 4

Subject Status by Treatment Group
All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Total Entered	533		269		802	
Not Treated	2	(0.4)	3	(1.1)	5	(0.6)
Treated	531	(99.6)	266	(98.9)	797	(99.4)
Discontinued Study	44	(8.3)	25	(9.3)	69	(8.6)
Adverse Event	6	(1.1)	6	(2.2)	12	(1.5)
Death	0	(0.0)	1	(0.4)	1	(0.1)
Lack Of Efficacy	4	(0.8)	1	(0.4)	5	(0.6)
Lost To Follow-Up	9	(1.7)	5	(1.9)	14	(1.7)
Non-Compliance With Study Drug	5	(0.9)	4	(1.5)	9	(1.1)
Physician Decision	5	(0.9)	0	(0.0)	5	(0.6)
Pregnancy	2	(0.4)	0	(0.0)	2	(0.2)
Withdrawal By Subject	13	(2.4)	8	(3.0)	21	(2.6)

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.
n (%)= Number (percent) of subjects in each sub-category.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 5

Subject Follow-up Time
Weeks 0-48

Follow-up Time	Raltegravir 1200 mg QD (N=531)	Raltegravir 400 mg BID (N=266)
Median (Range) (Weeks)	54.0 (3.3, 54.0)	54.0 (3.0, 54.0)
Mean (Weeks)	50.7	50.5
Total (Patient-Years)	515.6	257.7
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.		

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 6

Subject Baseline Characteristics by Treatment Group

	Raltegravir 1200 mg QD (N = 531)	Raltegravir 400 mg BID (N = 266)	Total (N = 797)
Gender n (%)			
Male	440 (82.9)	234 (88.0)	674 (84.6)
Female	91 (17.1)	32 (12.0)	123 (15.4)
Race n (%)			
American Indian or Alaska Native	3 (0.6)	3 (1.1)	6 (0.8)
Asian	83 (15.6)	40 (15.0)	123 (15.4)
Black or African American	98 (18.5)	36 (13.5)	134 (16.8)
Multiple	46 (8.7)	14 (5.3)	60 (7.5)
Native Hawaiian or Other Pacific Islander	0 (0.0)	1 (0.4)	1 (0.1)
White	301 (56.7)	172 (64.7)	473 (59.3)
Ethnicity n (%)			
Hispanic or Latino	126 (23.7)	52 (19.5)	178 (22.3)
Not Hispanic or Latino	380 (71.6)	205 (77.1)	585 (73.4)
Not Reported	19 (3.6)	8 (3.0)	27 (3.4)
Unknown	6 (1.1)	1 (0.4)	7 (0.9)
Region n (%)			
Africa	43 (8.1)	13 (4.9)	56 (7.0)
Asia/Pacific	86 (16.2)	46 (17.3)	132 (16.6)
Europe	200 (37.7)	112 (42.1)	312 (39.1)
Latin America	77 (14.5)	26 (9.8)	103 (12.9)
North America	125 (23.5)	69 (25.9)	194 (24.3)
Age (years)			
18 to 64	527 (99.2)	263 (98.9)	790 (99.1)
>=65	4 (0.8)	3 (1.1)	7 (0.9)
Mean (SD)	35.4 (10.3)	36.9 (11.0)	35.9 (10.5)
Median (min, max)	34.0 (18, 66)	35.0 (19, 84)	34.0 (18, 84)
Baseline CD4 Cell Count (cells/mm^3)			
N[†]	531	266	797
Mean (SD)	407.6 (213.7)	428.9 (217.3)	414.7 (215.0)
Median (min, max)	380.0 (19, 1836)	415.5 (19, 1130)	390.0 (19, 1836)
Baseline CD4 Cell Counts n (%)			
<=50 cells/mm^3	9 (1.7)	6 (2.3)	15 (1.9)
>50 cells/mm^3 and <=200 cells/mm^3	60 (11.3)	31 (11.7)	91 (11.4)
>200 cells/mm^3	462 (87.0)	229 (86.1)	691 (86.7)
Baseline Plasma HIV RNA (log10 copies/mL)			
N[†]	531	266	797
Mean (SD)	4.6 (0.7)	4.6 (0.7)	4.6 (0.7)
Median (min, max)	4.6 (1.6, 6.6)	4.6 (2.7, 6.2)	4.6 (1.6, 6.6)

Subject Baseline Characteristics by Treatment Group

	Raltegravir 1200 mg QD (N = 531)	Raltegravir 400 mg BID (N = 266)	Total (N = 797)
Baseline Plasma HIV RNA (copies/mL)			
N[†]	531	266	797
Geometric Mean	40518.8	40733.2	40590.2
Median (min, max)	43890.0 (39, 3910386)	40631.0 (454, 1466713)	42424.0 (39, 3910386)
Baseline Plasma HIV RNA n (%)			
<=100,000 copies/mL	382 (71.9)	189 (71.1)	571 (71.6)
>100,000 copies/mL	149 (28.1)	77 (28.9)	226 (28.4)
Baseline Plasma HIV RNA n (%)			
<=500,000 copies/mL	506 (95.3)	251 (94.4)	757 (95.0)
>500,000 copies/mL	25 (4.7)	15 (5.6)	40 (5.0)
History of AIDS n (%)			
Yes	79 (14.9)	28 (10.5)	107 (13.4)
No	452 (85.1)	238 (89.5)	690 (86.6)
Stratum n (%)			
Screening HIV RNA<= 100,000	382 (71.9)	190 (71.4)	572 (71.8)
Hepatitis B and/or C Positive[††]	15 (2.8)	8 (3.0)	23 (2.9)
Baseline Hepatitis Status			
Hep B Positive Only	11 (2.1)	3 (1.1)	14 (1.8)
Hep C Positive Only	4 (0.8)	4 (1.5)	8 (1.0)
Both Hep B and Hep C Positive	0 (0.0)	1 (0.4)	1 (0.1)
Viral Subtype n (%)			
Clade B	335 (63.1)	186 (69.9)	521 (65.4)
Non-Clade B	194 (36.5)	77 (28.9)	271 (34.0)
Missing	2 (0.4)	3 (1.1)	5 (0.6)

[†] Subjects with missing results excluded.

[††] Evidence of hepatitis B surface antigen or evidence of HCV RNA by polymerase chain reaction(PCR) quantitative test for hepatitis C Virus. 19 subjects previously classified as hepatitis B or C positive were subsequently identified based on lab tests as being hepatitis B or C negative. 3 subjects previously classified as hepatitis B or C negative were subsequently identified based on lab tests as being hepatitis B or C positive.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of patients randomized and treated in each treatment group.

n (%) = Number (percent) of patients in each sub-category.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 7

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
With one or more conditions	531	(100.0)	266	(100.0)	797	(100.0)
With no conditions	0	(0.0)	0	(0.0)	0	(0.0)
Blood and lymphatic system disorders	**73**	**(13.7)**	**38**	**(14.3)**	**111**	**(13.9)**
Anaemia	11	(2.1)	8	(3.0)	19	(2.4)
Anaemia macrocytic	1	(0.2)	0	(0.0)	1	(0.1)
Bicytopenia	0	(0.0)	1	(0.4)	1	(0.1)
Eosinophilia	0	(0.0)	1	(0.4)	1	(0.1)
Hilar lymphadenopathy	0	(0.0)	1	(0.4)	1	(0.1)
Immune thrombocytopenic purpura	0	(0.0)	2	(0.8)	2	(0.3)
Iron deficiency anaemia	5	(0.9)	1	(0.4)	6	(0.8)
Leukocytosis	0	(0.0)	1	(0.4)	1	(0.1)
Leukopenia	0	(0.0)	2	(0.8)	2	(0.3)
Lymph node calcification	1	(0.2)	0	(0.0)	1	(0.1)
Lymphadenitis	2	(0.4)	1	(0.4)	3	(0.4)
Lymphadenopathy	51	(9.6)	20	(7.5)	71	(8.9)
Lymphocytosis	0	(0.0)	1	(0.4)	1	(0.1)
Lymphopenia	0	(0.0)	1	(0.4)	1	(0.1)
Microcytic anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Monocytosis	0	(0.0)	1	(0.4)	1	(0.1)
Neutropenia	0	(0.0)	1	(0.4)	1	(0.1)
Normochromic normocytic anaemia	0	(0.0)	2	(0.8)	2	(0.3)
Pancytopenia	0	(0.0)	1	(0.4)	1	(0.1)
Sickle cell anaemia with crisis	1	(0.2)	0	(0.0)	1	(0.1)
Splenic cyst	1	(0.2)	0	(0.0)	1	(0.1)
Splenomegaly	2	(0.4)	2	(0.8)	4	(0.5)
Thrombocytopenia	4	(0.8)	3	(1.1)	7	(0.9)
Cardiac disorders	**18**	**(3.4)**	**4**	**(1.5)**	**22**	**(2.8)**
Acute myocardial infarction	1	(0.2)	0	(0.0)	1	(0.1)
Arrhythmia	1	(0.2)	1	(0.4)	2	(0.3)
Atrial fibrillation	5	(0.9)	0	(0.0)	5	(0.6)
Brugada syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Bundle branch block right	1	(0.2)	0	(0.0)	1	(0.1)
Cardiomyopathy	1	(0.2)	0	(0.0)	1	(0.1)
Coronary artery disease	2	(0.4)	0	(0.0)	2	(0.3)
Heart valve incompetence	1	(0.2)	0	(0.0)	1	(0.1)
Mitral valve prolapse	1	(0.2)	0	(0.0)	1	(0.1)
Myocardial infarction	0	(0.0)	1	(0.4)	1	(0.1)
Myocardial ischaemia	1	(0.2)	0	(0.0)	1	(0.1)
Palpitations	3	(0.6)	0	(0.0)	3	(0.4)
Sinus tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Supraventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Cardiac disorders	**18**	**(3.4)**	**4**	**(1.5)**	**22**	**(2.8)**
Tachycardia	3	(0.6)	2	(0.8)	5	(0.6)
Ventricular arrhythmia	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**16**	**(3.0)**	**8**	**(3.0)**	**24**	**(3.0)**
Bronchogenic cyst	0	(0.0)	1	(0.4)	1	(0.1)
Chondrodystrophy	1	(0.2)	0	(0.0)	1	(0.1)
Cleft lip and palate	1	(0.2)	0	(0.0)	1	(0.1)
Cryptorchism	2	(0.4)	0	(0.0)	2	(0.3)
Developmental hip dysplasia	0	(0.0)	1	(0.4)	1	(0.1)
Dextrocardia	0	(0.0)	1	(0.4)	1	(0.1)
Factor V deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Gilbert's syndrome	2	(0.4)	1	(0.4)	3	(0.4)
Glucose-6-phosphate dehydrogenase deficiency	0	(0.0)	1	(0.4)	1	(0.1)
Haemophilia	0	(0.0)	1	(0.4)	1	(0.1)
Keratosis follicular	0	(0.0)	1	(0.4)	1	(0.1)
Klinefelter's syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Phimosis	2	(0.4)	0	(0.0)	2	(0.3)
Renal aplasia	1	(0.2)	0	(0.0)	1	(0.1)
Sickle cell anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Spina bifida occulta	1	(0.2)	0	(0.0)	1	(0.1)
Syringomyelia	0	(0.0)	1	(0.4)	1	(0.1)
Thalassaemia	1	(0.2)	0	(0.0)	1	(0.1)
Thalassaemia alpha	0	(0.0)	1	(0.4)	1	(0.1)
Thalassaemia beta	1	(0.2)	0	(0.0)	1	(0.1)
Thalassaemia trait	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**17**	**(3.2)**	**8**	**(3.0)**	**25**	**(3.1)**
Cerumen impaction	1	(0.2)	1	(0.4)	2	(0.3)
Conductive deafness	1	(0.2)	0	(0.0)	1	(0.1)
Deafness	0	(0.0)	1	(0.4)	1	(0.1)
Deafness bilateral	1	(0.2)	0	(0.0)	1	(0.1)
Deafness neurosensory	1	(0.2)	0	(0.0)	1	(0.1)
Deafness unilateral	2	(0.4)	0	(0.0)	2	(0.3)
Ear discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Ear pain	2	(0.4)	1	(0.4)	3	(0.4)
Eustachian tube disorder	1	(0.2)	0	(0.0)	1	(0.1)
Excessive cerumen production	1	(0.2)	0	(0.0)	1	(0.1)
Hearing impaired	1	(0.2)	0	(0.0)	1	(0.1)
Hypoacusis	2	(0.4)	0	(0.0)	2	(0.3)
Middle ear inflammation	2	(0.4)	0	(0.0)	2	(0.3)
Tinnitus	4	(0.8)	0	(0.0)	4	(0.5)
Tympanic membrane disorder	0	(0.0)	1	(0.4)	1	(0.1)
Vertigo	2	(0.4)	4	(1.5)	6	(0.8)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Endocrine disorders	**15**	**(2.8)**	**9**	**(3.4)**	**24**	**(3.0)**
Androgen deficiency	1	(0.2)	1	(0.4)	2	(0.3)
Autoimmune thyroiditis	0	(0.0)	1	(0.4)	1	(0.1)
Basedow's disease	1	(0.2)	0	(0.0)	1	(0.1)
Goitre	5	(0.9)	1	(0.4)	6	(0.8)
Hyperparathyroidism secondary	1	(0.2)	0	(0.0)	1	(0.1)
Hypogonadism	0	(0.0)	4	(1.5)	4	(0.5)
Hypothyroidism	6	(1.1)	2	(0.8)	8	(1.0)
Secondary hypogonadism	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid disorder	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**23**	**(4.3)**	**16**	**(6.0)**	**39**	**(4.9)**
Astigmatism	1	(0.2)	1	(0.4)	2	(0.3)
Chorioretinopathy	2	(0.4)	0	(0.0)	2	(0.3)
Conjunctivitis allergic	2	(0.4)	1	(0.4)	3	(0.4)
Dry eye	1	(0.2)	1	(0.4)	2	(0.3)
Eyelids pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Glaucoma	1	(0.2)	0	(0.0)	1	(0.1)
Hypermetropia	3	(0.6)	2	(0.8)	5	(0.6)
Keratoconus	1	(0.2)	0	(0.0)	1	(0.1)
Myopia	5	(0.9)	5	(1.9)	10	(1.3)
Ocular discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Ocular hyperaemia	0	(0.0)	1	(0.4)	1	(0.1)
Ocular icterus	0	(0.0)	1	(0.4)	1	(0.1)
Ocular vascular disorder	0	(0.0)	1	(0.4)	1	(0.1)
Presbyopia	1	(0.2)	0	(0.0)	1	(0.1)
Retinal tear	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	3	(0.6)	0	(0.0)	3	(0.4)
Visual acuity reduced	1	(0.2)	2	(0.8)	3	(0.4)
Visual impairment	1	(0.2)	0	(0.0)	1	(0.1)
Vitreous degeneration	1	(0.2)	0	(0.0)	1	(0.1)
Vitreous floaters	1	(0.2)	1	(0.4)	2	(0.3)
Gastrointestinal disorders	**134**	**(25.2)**	**67**	**(25.2)**	**201**	**(25.2)**
Abdominal distension	4	(0.8)	2	(0.8)	6	(0.8)
Abdominal hernia	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain	7	(1.3)	4	(1.5)	11	(1.4)
Abdominal pain lower	1	(0.2)	0	(0.0)	1	(0.1)
Abdominal pain upper	2	(0.4)	0	(0.0)	2	(0.3)
Anal fissure	3	(0.6)	3	(1.1)	6	(0.8)
Anal fistula	1	(0.2)	2	(0.8)	3	(0.4)
Anal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Anal inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**134**	**(25.2)**	**67**	**(25.2)**	**201**	**(25.2)**
Anal skin tags	1	(0.2)	0	(0.0)	1	(0.1)
Anal stenosis	1	(0.2)	0	(0.0)	1	(0.1)
Anal ulcer	1	(0.2)	1	(0.4)	2	(0.3)
Anogenital dysplasia	5	(0.9)	2	(0.8)	7	(0.9)
Aphthous ulcer	4	(0.8)	2	(0.8)	6	(0.8)
Barrett's oesophagus	0	(0.0)	1	(0.4)	1	(0.1)
Chronic gastritis	4	(0.8)	1	(0.4)	5	(0.6)
Coeliac disease	1	(0.2)	0	(0.0)	1	(0.1)
Colitis	3	(0.6)	1	(0.4)	4	(0.5)
Colitis ulcerative	0	(0.0)	1	(0.4)	1	(0.1)
Constipation	9	(1.7)	4	(1.5)	13	(1.6)
Crohn's disease	0	(0.0)	1	(0.4)	1	(0.1)
Dental caries	8	(1.5)	1	(0.4)	9	(1.1)
Diarrhoea	24	(4.5)	12	(4.5)	36	(4.5)
Diverticulum intestinal	1	(0.2)	0	(0.0)	1	(0.1)
Dry mouth	1	(0.2)	1	(0.4)	2	(0.3)
Duodenitis haemorrhagic	1	(0.2)	0	(0.0)	1	(0.1)
Dyspepsia	11	(2.1)	9	(3.4)	20	(2.5)
Dysphagia	2	(0.4)	1	(0.4)	3	(0.4)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Erosive duodenitis	1	(0.2)	0	(0.0)	1	(0.1)
Faecaloma	0	(0.0)	1	(0.4)	1	(0.1)
Flatulence	2	(0.4)	1	(0.4)	3	(0.4)
Food poisoning	0	(0.0)	1	(0.4)	1	(0.1)
Gastric disorder	2	(0.4)	1	(0.4)	3	(0.4)
Gastric ulcer	2	(0.4)	2	(0.8)	4	(0.5)
Gastritis	12	(2.3)	2	(0.8)	14	(1.8)
Gastritis erosive	1	(0.2)	0	(0.0)	1	(0.1)
Gastroduodenitis	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorder	1	(0.2)	1	(0.4)	2	(0.3)
Gastrointestinal inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	16	(3.0)	8	(3.0)	24	(3.0)
Gingival bleeding	0	(0.0)	1	(0.4)	1	(0.1)
Gingival disorder	0	(0.0)	1	(0.4)	1	(0.1)
Glossodynia	1	(0.2)	0	(0.0)	1	(0.1)
Haematochezia	3	(0.6)	1	(0.4)	4	(0.5)
Haemorrhoidal haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoids	15	(2.8)	8	(3.0)	23	(2.9)
Haemorrhoids thrombosed	3	(0.6)	0	(0.0)	3	(0.4)
Hiatus hernia	2	(0.4)	0	(0.0)	2	(0.3)
Inguinal hernia	9	(1.7)	5	(1.9)	14	(1.8)
Irritable bowel syndrome	1	(0.2)	4	(1.5)	5	(0.6)
Large intestinal ulcer	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**134**	**(25.2)**	**67**	**(25.2)**	**201**	**(25.2)**
Large intestine polyp	2	(0.4)	0	(0.0)	2	(0.3)
Lip disorder	0	(0.0)	1	(0.4)	1	(0.1)
Lumbar hernia	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	2	(0.4)	2	(0.8)	4	(0.5)
Nausea	4	(0.8)	3	(1.1)	7	(0.9)
Noninfective gingivitis	1	(0.2)	1	(0.4)	2	(0.3)
Odynophagia	0	(0.0)	1	(0.4)	1	(0.1)
Oesophageal stenosis	1	(0.2)	0	(0.0)	1	(0.1)
Oesophagitis	1	(0.2)	1	(0.4)	2	(0.3)
Pancreatic steatosis	2	(0.4)	0	(0.0)	2	(0.3)
Pancreatitis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis chronic	1	(0.2)	0	(0.0)	1	(0.1)
Perianal erythema	1	(0.2)	0	(0.0)	1	(0.1)
Periodontal disease	0	(0.0)	1	(0.4)	1	(0.1)
Proctalgia	3	(0.6)	1	(0.4)	4	(0.5)
Proctitis	4	(0.8)	3	(1.1)	7	(0.9)
Pseudodiverticular disease	1	(0.2)	0	(0.0)	1	(0.1)
Rectal haemorrhage	1	(0.2)	1	(0.4)	2	(0.3)
Salivary gland cyst	1	(0.2)	0	(0.0)	1	(0.1)
Salivary gland mucocoele	1	(0.2)	0	(0.0)	1	(0.1)
Supernumerary teeth	0	(0.0)	1	(0.4)	1	(0.1)
Tongue ulceration	1	(0.2)	0	(0.0)	1	(0.1)
Tooth disorder	0	(0.0)	2	(0.8)	2	(0.3)
Tooth loss	0	(0.0)	1	(0.4)	1	(0.1)
Toothache	1	(0.2)	1	(0.4)	2	(0.3)
Umbilical hernia	0	(0.0)	1	(0.4)	1	(0.1)
Vomiting	2	(0.4)	3	(1.1)	5	(0.6)
General disorders and administration site conditions	**32**	**(6.0)**	**22**	**(8.3)**	**54**	**(6.8)**
Adverse drug reaction	1	(0.2)	0	(0.0)	1	(0.1)
Asthenia	3	(0.6)	1	(0.4)	4	(0.5)
Calcinosis	0	(0.0)	1	(0.4)	1	(0.1)
Chest pain	3	(0.6)	0	(0.0)	3	(0.4)
Fatigue	16	(3.0)	14	(5.3)	30	(3.8)
Fibrosis	1	(0.2)	0	(0.0)	1	(0.1)
General symptom	1	(0.2)	0	(0.0)	1	(0.1)
Inflammatory pain	1	(0.2)	0	(0.0)	1	(0.1)
Influenza like illness	0	(0.0)	1	(0.4)	1	(0.1)
Nodule	1	(0.2)	0	(0.0)	1	(0.1)
Pain	2	(0.4)	2	(0.8)	4	(0.5)
Peripheral swelling	1	(0.2)	1	(0.4)	2	(0.3)
Pyrexia	4	(0.8)	7	(2.6)	11	(1.4)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Hepatobiliary disorders	**15**	**(2.8)**	**10**	**(3.8)**	**25**	**(3.1)**
Biliary dyskinesia	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystitis	3	(0.6)	0	(0.0)	3	(0.4)
Cholecystitis chronic	1	(0.2)	0	(0.0)	1	(0.1)
Cholelithiasis	4	(0.8)	2	(0.8)	6	(0.8)
Cholestasis	1	(0.2)	0	(0.0)	1	(0.1)
Drug-induced liver injury	1	(0.2)	0	(0.0)	1	(0.1)
Gallbladder polyp	0	(0.0)	1	(0.4)	1	(0.1)
Gallbladder volvulus	0	(0.0)	1	(0.4)	1	(0.1)
Hepatic function abnormal	1	(0.2)	0	(0.0)	1	(0.1)
Hepatic steatosis	3	(0.6)	3	(1.1)	6	(0.8)
Hepatomegaly	4	(0.8)	0	(0.0)	4	(0.5)
Hepatosplenomegaly	0	(0.0)	1	(0.4)	1	(0.1)
Hyperbilirubinaemia	0	(0.0)	2	(0.8)	2	(0.3)
Hypertransaminasaemia	0	(0.0)	1	(0.4)	1	(0.1)
Liver injury	1	(0.2)	0	(0.0)	1	(0.1)
Immune system disorders	**68**	**(12.8)**	**45**	**(16.9)**	**113**	**(14.2)**
Allergy to animal	5	(0.9)	3	(1.1)	8	(1.0)
Allergy to arthropod sting	1	(0.2)	0	(0.0)	1	(0.1)
Allergy to chemicals	3	(0.6)	0	(0.0)	3	(0.4)
Allergy to metals	1	(0.2)	0	(0.0)	1	(0.1)
Anaphylactic reaction	2	(0.4)	1	(0.4)	3	(0.4)
Contrast media allergy	0	(0.0)	1	(0.4)	1	(0.1)
Drug hypersensitivity	26	(4.9)	17	(6.4)	43	(5.4)
Food allergy	4	(0.8)	5	(1.9)	9	(1.1)
House dust allergy	2	(0.4)	2	(0.8)	4	(0.5)
Hypersensitivity	2	(0.4)	2	(0.8)	4	(0.5)
Immune reconstitution inflammatory syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Milk allergy	1	(0.2)	0	(0.0)	1	(0.1)
Reaction to food additive	1	(0.2)	0	(0.0)	1	(0.1)
Rubber sensitivity	0	(0.0)	1	(0.4)	1	(0.1)
Seasonal allergy	32	(6.0)	20	(7.5)	52	(6.5)
Infections and infestations	**531**	**(100.0)**	**266**	**(100.0)**	**797**	**(100.0)**
AIDS dementia complex	1	(0.2)	0	(0.0)	1	(0.1)
Abscess limb	2	(0.4)	0	(0.0)	2	(0.3)
Acarodermatitis	2	(0.4)	3	(1.1)	5	(0.6)
Acquired immunodeficiency syndrome	79	(14.9)	28	(10.5)	107	(13.4)
Acute HIV infection	0	(0.0)	3	(1.1)	3	(0.4)
Acute hepatitis B	1	(0.2)	0	(0.0)	1	(0.1)
Amoebiasis	1	(0.2)	0	(0.0)	1	(0.1)
Anal abscess	2	(0.4)	3	(1.1)	5	(0.6)
Anal chlamydia infection	2	(0.4)	0	(0.0)	2	(0.3)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**531**	**(100.0)**	**266**	**(100.0)**	**797**	**(100.0)**
Angular cheilitis	2	(0.4)	1	(0.4)	3	(0.4)
Anorectal cellulitis	0	(0.0)	1	(0.4)	1	(0.1)
Anorectal infection bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Appendicitis	10	(1.9)	1	(0.4)	11	(1.4)
Arthritis bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Bacterial diarrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Bacterial vaginosis	1	(0.2)	0	(0.0)	1	(0.1)
Balanitis candida	2	(0.4)	0	(0.0)	2	(0.3)
Blastocystis infection	1	(0.2)	0	(0.0)	1	(0.1)
Body tinea	3	(0.6)	0	(0.0)	3	(0.4)
Bronchitis	7	(1.3)	3	(1.1)	10	(1.3)
Candida infection	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	3	(0.6)	0	(0.0)	3	(0.4)
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)	1	(0.1)
Chest wall abscess	1	(0.2)	0	(0.0)	1	(0.1)
Chlamydial infection	9	(1.7)	5	(1.9)	14	(1.8)
Cholecystitis infective	1	(0.2)	0	(0.0)	1	(0.1)
Chorioretinitis	0	(0.0)	1	(0.4)	1	(0.1)
Chronic hepatitis B	12	(2.3)	1	(0.4)	13	(1.6)
Chronic hepatitis C	11	(2.1)	6	(2.3)	17	(2.1)
Chronic sinusitis	3	(0.6)	2	(0.8)	5	(0.6)
Conjunctivitis	2	(0.4)	0	(0.0)	2	(0.3)
Coxsackie pericarditis	1	(0.2)	0	(0.0)	1	(0.1)
Cryptococcosis	0	(0.0)	1	(0.4)	1	(0.1)
Cryptosporidiosis infection	0	(0.0)	1	(0.4)	1	(0.1)
Cystitis	1	(0.2)	0	(0.0)	1	(0.1)
Cytomegalovirus infection	2	(0.4)	0	(0.0)	2	(0.3)
Dengue fever	4	(0.8)	1	(0.4)	5	(0.6)
Dermatophytosis of nail	4	(0.8)	0	(0.0)	4	(0.5)
Diverticulitis	2	(0.4)	2	(0.8)	4	(0.5)
Ear infection	1	(0.2)	1	(0.4)	2	(0.3)
Enterocolitis bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Epididymitis	1	(0.2)	2	(0.8)	3	(0.4)
Epstein-Barr virus infection	1	(0.2)	0	(0.0)	1	(0.1)
Eye infection	1	(0.2)	0	(0.0)	1	(0.1)
Eye infection syphilitic	1	(0.2)	0	(0.0)	1	(0.1)
Folliculitis	3	(0.6)	3	(1.1)	6	(0.8)
Fungal infection	1	(0.2)	1	(0.4)	2	(0.3)
Fungal skin infection	2	(0.4)	1	(0.4)	3	(0.4)
Furuncle	3	(0.6)	3	(1.1)	6	(0.8)
Gastroenteritis	3	(0.6)	1	(0.4)	4	(0.5)
Gastroenteritis cryptosporidial	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis salmonella	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**531**	**(100.0)**	**266**	**(100.0)**	**797**	**(100.0)**
Genital herpes	8	(1.5)	2	(0.8)	10	(1.3)
Genital herpes simplex	2	(0.4)	2	(0.8)	4	(0.5)
Genitourinary chlamydia infection	0	(0.0)	1	(0.4)	1	(0.1)
Giardiasis	0	(0.0)	1	(0.4)	1	(0.1)
Gingivitis	2	(0.4)	2	(0.8)	4	(0.5)
Gonorrhoea	20	(3.8)	9	(3.4)	29	(3.6)
Groin abscess	1	(0.2)	0	(0.0)	1	(0.1)
HIV infection	531	(100.0)	266	(100.0)	797	(100.0)
HIV wasting syndrome	2	(0.4)	2	(0.8)	4	(0.5)
Helicobacter infection	1	(0.2)	1	(0.4)	2	(0.3)
Hepatic amoebiasis	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis A	8	(1.5)	6	(2.3)	14	(1.8)
Hepatitis B	19	(3.6)	14	(5.3)	33	(4.1)
Hepatitis C	5	(0.9)	2	(0.8)	7	(0.9)
Hepatitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Herpes dermatitis	0	(0.0)	1	(0.4)	1	(0.1)
Herpes ophthalmic	1	(0.2)	1	(0.4)	2	(0.3)
Herpes pharyngitis	0	(0.0)	1	(0.4)	1	(0.1)
Herpes simplex	15	(2.8)	8	(3.0)	23	(2.9)
Herpes virus infection	2	(0.4)	1	(0.4)	3	(0.4)
Herpes zoster	22	(4.1)	15	(5.6)	37	(4.6)
Hordeolum	2	(0.4)	0	(0.0)	2	(0.3)
Impetigo	1	(0.2)	1	(0.4)	2	(0.3)
Infectious colitis	1	(0.2)	0	(0.0)	1	(0.1)
Influenza	5	(0.9)	0	(0.0)	5	(0.6)
Joint abscess	0	(0.0)	1	(0.4)	1	(0.1)
Laryngitis	1	(0.2)	0	(0.0)	1	(0.1)
Laryngitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Latent syphilis	12	(2.3)	5	(1.9)	17	(2.1)
Latent tuberculosis	1	(0.2)	3	(1.1)	4	(0.5)
Lower respiratory tract infection	2	(0.4)	2	(0.8)	4	(0.5)
Malaria	3	(0.6)	0	(0.0)	3	(0.4)
Mastoiditis	1	(0.2)	0	(0.0)	1	(0.1)
Meningitis	3	(0.6)	1	(0.4)	4	(0.5)
Meningitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Mononucleosis syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Mycobacterium avium complex infection	0	(0.0)	1	(0.4)	1	(0.1)
Myringitis	1	(0.2)	0	(0.0)	1	(0.1)
Nail infection	1	(0.2)	0	(0.0)	1	(0.1)
Nasopharyngitis	5	(0.9)	0	(0.0)	5	(0.6)
Nematodiasis	1	(0.2)	0	(0.0)	1	(0.1)
Oesophageal candidiasis	1	(0.2)	3	(1.1)	4	(0.5)
Onychomycosis	14	(2.6)	5	(1.9)	19	(2.4)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**531**	**(100.0)**	**266**	**(100.0)**	**797**	**(100.0)**
Ophthalmic herpes simplex	0	(0.0)	1	(0.4)	1	(0.1)
Ophthalmic herpes zoster	0	(0.0)	2	(0.8)	2	(0.3)
Oral candidiasis	11	(2.1)	14	(5.3)	25	(3.1)
Oral fungal infection	1	(0.2)	0	(0.0)	1	(0.1)
Oral hairy leukoplakia	7	(1.3)	3	(1.1)	10	(1.3)
Oral herpes	10	(1.9)	4	(1.5)	14	(1.8)
Orchitis	1	(0.2)	2	(0.8)	3	(0.4)
Oropharyngeal gonococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Otitis externa	3	(0.6)	0	(0.0)	3	(0.4)
Otitis media	2	(0.4)	0	(0.0)	2	(0.3)
Papilloma viral infection	2	(0.4)	0	(0.0)	2	(0.3)
Paronychia	1	(0.2)	0	(0.0)	1	(0.1)
Periodontitis	1	(0.2)	0	(0.0)	1	(0.1)
Peritonitis	1	(0.2)	0	(0.0)	1	(0.1)
Persistent generalised lymphadenopathy	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngitis	8	(1.5)	2	(0.8)	10	(1.3)
Pharyngitis streptococcal	2	(0.4)	0	(0.0)	2	(0.3)
Pharyngotonsillitis	1	(0.2)	1	(0.4)	2	(0.3)
Pilonidal cyst	1	(0.2)	0	(0.0)	1	(0.1)
Pneumocystis jirovecii pneumonia	5	(0.9)	2	(0.8)	7	(0.9)
Pneumonia	7	(1.3)	3	(1.1)	10	(1.3)
Primary syphilis	2	(0.4)	0	(0.0)	2	(0.3)
Proctitis chlamydial	4	(0.8)	2	(0.8)	6	(0.8)
Proctitis gonococcal	2	(0.4)	1	(0.4)	3	(0.4)
Proctitis herpes	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary tuberculoma	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary tuberculosis	2	(0.4)	3	(1.1)	5	(0.6)
Rash pustular	3	(0.6)	0	(0.0)	3	(0.4)
Rectal abscess	1	(0.2)	1	(0.4)	2	(0.3)
Respiratory tract infection	0	(0.0)	1	(0.4)	1	(0.1)
Respiratory tract infection viral	1	(0.2)	1	(0.4)	2	(0.3)
Rhinitis	3	(0.6)	0	(0.0)	3	(0.4)
Secondary syphilis	6	(1.1)	2	(0.8)	8	(1.0)
Shigella infection	0	(0.0)	2	(0.8)	2	(0.3)
Sinusitis	8	(1.5)	4	(1.5)	12	(1.5)
Skin candida	0	(0.0)	2	(0.8)	2	(0.3)
Small intestinal bacterial overgrowth	0	(0.0)	1	(0.4)	1	(0.1)
Staphylococcal pharyngitis	0	(0.0)	1	(0.4)	1	(0.1)
Subcutaneous abscess	2	(0.4)	2	(0.8)	4	(0.5)
Syphilis	69	(13.0)	35	(13.2)	104	(13.0)
Syphilis genital	1	(0.2)	0	(0.0)	1	(0.1)
Tinea cruris	2	(0.4)	0	(0.0)	2	(0.3)
Tinea infection	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**531**	**(100.0)**	**266**	**(100.0)**	**797**	**(100.0)**
Tinea pedis	2	(0.4)	2	(0.8)	4	(0.5)
Tinea versicolour	1	(0.2)	2	(0.8)	3	(0.4)
Tonsillitis	13	(2.4)	4	(1.5)	17	(2.1)
Tonsillitis streptococcal	1	(0.2)	0	(0.0)	1	(0.1)
Tooth abscess	1	(0.2)	0	(0.0)	1	(0.1)
Tooth infection	1	(0.2)	0	(0.0)	1	(0.1)
Trichomoniasis	2	(0.4)	0	(0.0)	2	(0.3)
Tuberculosis	3	(0.6)	1	(0.4)	4	(0.5)
Typhus	1	(0.2)	0	(0.0)	1	(0.1)
Upper respiratory tract infection	8	(1.5)	4	(1.5)	12	(1.5)
Urethritis	2	(0.4)	3	(1.1)	5	(0.6)
Urethritis chlamydial	2	(0.4)	0	(0.0)	2	(0.3)
Urethritis gonococcal	4	(0.8)	2	(0.8)	6	(0.8)
Urinary tract infection	8	(1.5)	2	(0.8)	10	(1.3)
Vaginal infection	0	(0.0)	1	(0.4)	1	(0.1)
Varicella	1	(0.2)	1	(0.4)	2	(0.3)
Varicella zoster virus infection	0	(0.0)	2	(0.8)	2	(0.3)
Viral infection	2	(0.4)	2	(0.8)	4	(0.5)
Viral rash	1	(0.2)	0	(0.0)	1	(0.1)
Vulvitis	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal candidiasis	2	(0.4)	0	(0.0)	2	(0.3)
Vulvovaginal mycotic infection	1	(0.2)	0	(0.0)	1	(0.1)
Injury, poisoning and procedural complications	**45**	**(8.5)**	**24**	**(9.0)**	**69**	**(8.7)**
Ankle fracture	1	(0.2)	0	(0.0)	1	(0.1)
Arthropod bite	1	(0.2)	1	(0.4)	2	(0.3)
Brain contusion	1	(0.2)	0	(0.0)	1	(0.1)
Cervical vertebral fracture	0	(0.0)	1	(0.4)	1	(0.1)
Chemical poisoning	1	(0.2)	0	(0.0)	1	(0.1)
Clavicle fracture	1	(0.2)	0	(0.0)	1	(0.1)
Concussion	0	(0.0)	2	(0.8)	2	(0.3)
Contusion	1	(0.2)	0	(0.0)	1	(0.1)
Dermatitis artefacta	0	(0.0)	1	(0.4)	1	(0.1)
Ear canal abrasion	0	(0.0)	1	(0.4)	1	(0.1)
Epicondylitis	2	(0.4)	0	(0.0)	2	(0.3)
Excoriation	0	(0.0)	1	(0.4)	1	(0.1)
Eye injury	1	(0.2)	0	(0.0)	1	(0.1)
Facial bones fracture	0	(0.0)	1	(0.4)	1	(0.1)
Femur fracture	0	(0.0)	2	(0.8)	2	(0.3)
Fibula fracture	0	(0.0)	1	(0.4)	1	(0.1)
Foot fracture	1	(0.2)	0	(0.0)	1	(0.1)
Forearm fracture	2	(0.4)	0	(0.0)	2	(0.3)
Hand fracture	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**45**	**(8.5)**	**24**	**(9.0)**	**69**	**(8.7)**
Head injury	2	(0.4)	1	(0.4)	3	(0.4)
Hip fracture	1	(0.2)	0	(0.0)	1	(0.1)
Humerus fracture	1	(0.2)	0	(0.0)	1	(0.1)
Incisional hernia	1	(0.2)	0	(0.0)	1	(0.1)
Joint dislocation	2	(0.4)	1	(0.4)	3	(0.4)
Joint injury	1	(0.2)	1	(0.4)	2	(0.3)
Laceration	2	(0.4)	0	(0.0)	2	(0.3)
Ligament rupture	1	(0.2)	1	(0.4)	2	(0.3)
Ligament sprain	4	(0.8)	0	(0.0)	4	(0.5)
Limb injury	0	(0.0)	1	(0.4)	1	(0.1)
Lumbar vertebral fracture	0	(0.0)	1	(0.4)	1	(0.1)
Meniscus injury	1	(0.2)	1	(0.4)	2	(0.3)
Mouth injury	0	(0.0)	1	(0.4)	1	(0.1)
Multiple fractures	0	(0.0)	1	(0.4)	1	(0.1)
Multiple injuries	1	(0.2)	0	(0.0)	1	(0.1)
Muscle strain	3	(0.6)	0	(0.0)	3	(0.4)
Optic nerve injury	0	(0.0)	1	(0.4)	1	(0.1)
Overdose	0	(0.0)	1	(0.4)	1	(0.1)
Post-traumatic neck syndrome	2	(0.4)	0	(0.0)	2	(0.3)
Radius fracture	1	(0.2)	1	(0.4)	2	(0.3)
Rib fracture	1	(0.2)	1	(0.4)	2	(0.3)
Road traffic accident	2	(0.4)	0	(0.0)	2	(0.3)
Scar	5	(0.9)	1	(0.4)	6	(0.8)
Scratch	1	(0.2)	0	(0.0)	1	(0.1)
Skull fracture	0	(0.0)	1	(0.4)	1	(0.1)
Soft tissue injury	1	(0.2)	0	(0.0)	1	(0.1)
Spinal column injury	0	(0.0)	1	(0.4)	1	(0.1)
Tendon injury	1	(0.2)	0	(0.0)	1	(0.1)
Thermal burn	2	(0.4)	1	(0.4)	3	(0.4)
Tibia fracture	0	(0.0)	1	(0.4)	1	(0.1)
Tooth fracture	1	(0.2)	0	(0.0)	1	(0.1)
Traumatic fracture	1	(0.2)	0	(0.0)	1	(0.1)
Upper limb fracture	1	(0.2)	0	(0.0)	1	(0.1)
Wound	2	(0.4)	0	(0.0)	2	(0.3)
Wrist fracture	1	(0.2)	0	(0.0)	1	(0.1)
Investigations	**70**	**(13.2)**	**32**	**(12.0)**	**102**	**(12.8)**
Alanine aminotransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Biopsy prostate	0	(0.0)	1	(0.4)	1	(0.1)
Blood HIV RNA decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood bilirubin increased	2	(0.4)	1	(0.4)	3	(0.4)
Blood cholesterol increased	1	(0.2)	3	(1.1)	4	(0.5)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**70**	**(13.2)**	**32**	**(12.0)**	**102**	**(12.8)**
Blood glucose abnormal	1	(0.2)	0	(0.0)	1	(0.1)
Blood glucose increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood pressure increased	2	(0.4)	2	(0.8)	4	(0.5)
Blood testosterone decreased	1	(0.2)	0	(0.0)	1	(0.1)
Body mass index increased	1	(0.2)	0	(0.0)	1	(0.1)
CD4 lymphocyte percentage decreased	22	(4.1)	6	(2.3)	28	(3.5)
CD4 lymphocytes decreased	22	(4.1)	6	(2.3)	28	(3.5)
Cardiac murmur	3	(0.6)	1	(0.4)	4	(0.5)
Carotid bruit	1	(0.2)	0	(0.0)	1	(0.1)
Catheterisation cardiac	1	(0.2)	0	(0.0)	1	(0.1)
Computerised tomogram thorax abnormal	1	(0.2)	0	(0.0)	1	(0.1)
Cystatin C increased	0	(0.0)	1	(0.4)	1	(0.1)
Cytology abnormal	0	(0.0)	1	(0.4)	1	(0.1)
Cytomegalovirus test positive	3	(0.6)	0	(0.0)	3	(0.4)
Glomerular filtration rate decreased	0	(0.0)	1	(0.4)	1	(0.1)
Haemoglobin decreased	2	(0.4)	1	(0.4)	3	(0.4)
Heart rate irregular	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis A virus test positive	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis B surface antibody	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis B surface antibody positive	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis B surface antigen	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis B virus test positive	0	(0.0)	1	(0.4)	1	(0.1)
Herpes simplex serology positive	0	(0.0)	1	(0.4)	1	(0.1)
Lipase increased	1	(0.2)	0	(0.0)	1	(0.1)
Liver function test abnormal	1	(0.2)	1	(0.4)	2	(0.3)
Liver scan abnormal	1	(0.2)	0	(0.0)	1	(0.1)
Lymph node palpable	1	(0.2)	0	(0.0)	1	(0.1)
Toxoplasma serology positive	1	(0.2)	0	(0.0)	1	(0.1)
Transaminases increased	0	(0.0)	2	(0.8)	2	(0.3)
Tuberculin test positive	1	(0.2)	1	(0.4)	2	(0.3)
Ultrasound abdomen	0	(0.0)	1	(0.4)	1	(0.1)
Weight decreased	12	(2.3)	6	(2.3)	18	(2.3)
Weight increased	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**78**	**(14.7)**	**32**	**(12.0)**	**110**	**(13.8)**
Central obesity	1	(0.2)	0	(0.0)	1	(0.1)
Decreased appetite	5	(0.9)	3	(1.1)	8	(1.0)
Diabetes mellitus	6	(1.1)	2	(0.8)	8	(1.0)
Dyslipidaemia	6	(1.1)	1	(0.4)	7	(0.9)
Glucose tolerance impaired	1	(0.2)	1	(0.4)	2	(0.3)
Gout	1	(0.2)	2	(0.8)	3	(0.4)
Hypercholesterolaemia	11	(2.1)	5	(1.9)	16	(2.0)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**78**	**(14.7)**	**32**	**(12.0)**	**110**	**(13.8)**
Hyperinsulinism	0	(0.0)	1	(0.4)	1	(0.1)
Hyperlipidaemia	9	(1.7)	3	(1.1)	12	(1.5)
Hyperproteinaemia	0	(0.0)	1	(0.4)	1	(0.1)
Hypertriglyceridaemia	7	(1.3)	2	(0.8)	9	(1.1)
Hyperuricaemia	4	(0.8)	0	(0.0)	4	(0.5)
Hypoalbuminaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypophosphataemia	0	(0.0)	1	(0.4)	1	(0.1)
Lactose intolerance	4	(0.8)	2	(0.8)	6	(0.8)
Malnutrition	1	(0.2)	0	(0.0)	1	(0.1)
Obesity	11	(2.1)	5	(1.9)	16	(2.0)
Overweight	2	(0.4)	0	(0.0)	2	(0.3)
Type 1 diabetes mellitus	0	(0.0)	1	(0.4)	1	(0.1)
Type 2 diabetes mellitus	4	(0.8)	1	(0.4)	5	(0.6)
Vitamin D deficiency	18	(3.4)	8	(3.0)	26	(3.3)
Weight fluctuation	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal and connective tissue disorders	**70**	**(13.2)**	**42**	**(15.8)**	**112**	**(14.1)**
Arthralgia	16	(3.0)	9	(3.4)	25	(3.1)
Arthritis	3	(0.6)	2	(0.8)	5	(0.6)
Arthritis reactive	1	(0.2)	0	(0.0)	1	(0.1)
Back pain	21	(4.0)	11	(4.1)	32	(4.0)
Bone pain	1	(0.2)	0	(0.0)	1	(0.1)
Chest wall cyst	1	(0.2)	0	(0.0)	1	(0.1)
Femoroacetabular impingement	1	(0.2)	0	(0.0)	1	(0.1)
Fibromyalgia	1	(0.2)	0	(0.0)	1	(0.1)
Foot deformity	2	(0.4)	2	(0.8)	4	(0.5)
Intervertebral disc protrusion	4	(0.8)	3	(1.1)	7	(0.9)
Joint stiffness	2	(0.4)	0	(0.0)	2	(0.3)
Joint swelling	1	(0.2)	0	(0.0)	1	(0.1)
Juvenile idiopathic arthritis	1	(0.2)	0	(0.0)	1	(0.1)
Kyphoscoliosis	1	(0.2)	0	(0.0)	1	(0.1)
Limb discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Muscle spasms	6	(1.1)	2	(0.8)	8	(1.0)
Muscular weakness	0	(0.0)	1	(0.4)	1	(0.1)
Musculoskeletal chest pain	2	(0.4)	0	(0.0)	2	(0.3)
Musculoskeletal pain	4	(0.8)	3	(1.1)	7	(0.9)
Myalgia	7	(1.3)	1	(0.4)	8	(1.0)
Myofascial pain syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Myositis	1	(0.2)	0	(0.0)	1	(0.1)
Neck mass	1	(0.2)	0	(0.0)	1	(0.1)
Neck pain	1	(0.2)	3	(1.1)	4	(0.5)
Osteoarthritis	6	(1.1)	4	(1.5)	10	(1.3)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**70**	**(13.2)**	**42**	**(15.8)**	**112**	**(14.1)**
Osteopenia	2	(0.4)	2	(0.8)	4	(0.5)
Pain in extremity	3	(0.6)	3	(1.1)	6	(0.8)
Patellofemoral pain syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Periarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Plantar fasciitis	2	(0.4)	1	(0.4)	3	(0.4)
Polyarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Rotator cuff syndrome	4	(0.8)	0	(0.0)	4	(0.5)
Scoliosis	4	(0.8)	2	(0.8)	6	(0.8)
Soft tissue disorder	0	(0.0)	1	(0.4)	1	(0.1)
Spinal column stenosis	1	(0.2)	0	(0.0)	1	(0.1)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Synovial cyst	3	(0.6)	2	(0.8)	5	(0.6)
Synovitis	1	(0.2)	1	(0.4)	2	(0.3)
Systemic lupus erythematosus	0	(0.0)	1	(0.4)	1	(0.1)
Tendon disorder	2	(0.4)	0	(0.0)	2	(0.3)
Tendonitis	1	(0.2)	0	(0.0)	1	(0.1)
Torticollis	0	(0.0)	1	(0.4)	1	(0.1)
Vertebral osteophyte	0	(0.0)	1	(0.4)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**57**	**(10.7)**	**35**	**(13.2)**	**92**	**(11.5)**
Abdominal wall neoplasm	0	(0.0)	1	(0.4)	1	(0.1)
Acrochordon	1	(0.2)	0	(0.0)	1	(0.1)
Anal cancer stage 0	0	(0.0)	1	(0.4)	1	(0.1)
Anogenital warts	31	(5.8)	14	(5.3)	45	(5.6)
Basal cell carcinoma	5	(0.9)	1	(0.4)	6	(0.8)
Benign bone neoplasm	0	(0.0)	1	(0.4)	1	(0.1)
Benign neoplasm of eye	0	(0.0)	1	(0.4)	1	(0.1)
Bowen's disease	0	(0.0)	1	(0.4)	1	(0.1)
Colon adenoma	1	(0.2)	0	(0.0)	1	(0.1)
Colon cancer	0	(0.0)	1	(0.4)	1	(0.1)
Diffuse large B-cell lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Fibroma	1	(0.2)	0	(0.0)	1	(0.1)
Fibrous histiocytoma	1	(0.2)	1	(0.4)	2	(0.3)
Haemangioma	0	(0.0)	2	(0.8)	2	(0.3)
Haemangioma of liver	1	(0.2)	0	(0.0)	1	(0.1)
Kaposi's sarcoma AIDS related	0	(0.0)	1	(0.4)	1	(0.1)
Large intestine benign neoplasm	3	(0.6)	0	(0.0)	3	(0.4)
Leiomyoma	0	(0.0)	1	(0.4)	1	(0.1)
Lipoma	1	(0.2)	0	(0.0)	1	(0.1)
Malignant melanoma	0	(0.0)	1	(0.4)	1	(0.1)
Melanocytic naevus	3	(0.6)	2	(0.8)	5	(0.6)
Mucoepidermoid carcinoma	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**57**	**(10.7)**	**35**	**(13.2)**	**92**	**(11.5)**
Nasal cavity cancer	1	(0.2)	0	(0.0)	1	(0.1)
Neuroma	0	(0.0)	1	(0.4)	1	(0.1)
Oral papilloma	0	(0.0)	1	(0.4)	1	(0.1)
Penile wart	1	(0.2)	0	(0.0)	1	(0.1)
Prostate cancer	0	(0.0)	1	(0.4)	1	(0.1)
Skin papilloma	6	(1.1)	6	(2.3)	12	(1.5)
Sweat gland tumour	1	(0.2)	0	(0.0)	1	(0.1)
Synovial sarcoma	0	(0.0)	1	(0.4)	1	(0.1)
Thyroid cancer	1	(0.2)	0	(0.0)	1	(0.1)
Thyroid neoplasm	0	(0.0)	1	(0.4)	1	(0.1)
Uterine leiomyoma	2	(0.4)	0	(0.0)	2	(0.3)
Vocal cord neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Vulvovaginal warts	0	(0.0)	2	(0.8)	2	(0.3)
Nervous system disorders	**76**	**(14.3)**	**46**	**(17.3)**	**122**	**(15.3)**
Ageusia	1	(0.2)	0	(0.0)	1	(0.1)
Apraxia	0	(0.0)	1	(0.4)	1	(0.1)
Arachnoid cyst	0	(0.0)	1	(0.4)	1	(0.1)
Carotid artery stenosis	1	(0.2)	1	(0.4)	2	(0.3)
Carpal tunnel syndrome	2	(0.4)	0	(0.0)	2	(0.3)
Cauda equina syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Cerebrovascular accident	1	(0.2)	1	(0.4)	2	(0.3)
Cervical radiculopathy	1	(0.2)	0	(0.0)	1	(0.1)
Cervicobrachial syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Coordination abnormal	0	(0.0)	1	(0.4)	1	(0.1)
Disturbance in attention	0	(0.0)	4	(1.5)	4	(0.5)
Dizziness	6	(1.1)	3	(1.1)	9	(1.1)
Epilepsy	4	(0.8)	3	(1.1)	7	(0.9)
Essential tremor	1	(0.2)	1	(0.4)	2	(0.3)
Generalised tonic-clonic seizure	0	(0.0)	2	(0.8)	2	(0.3)
Headache	31	(5.8)	20	(7.5)	51	(6.4)
Hemiparesis	0	(0.0)	1	(0.4)	1	(0.1)
Hydrocephalus	1	(0.2)	0	(0.0)	1	(0.1)
Hypertonia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	0	(0.0)	1	(0.4)	1	(0.1)
Hyposmia	0	(0.0)	1	(0.4)	1	(0.1)
Intracranial aneurysm	1	(0.2)	0	(0.0)	1	(0.1)
Intracranial pressure increased	0	(0.0)	1	(0.4)	1	(0.1)
Migraine	8	(1.5)	5	(1.9)	13	(1.6)
Migraine with aura	0	(0.0)	1	(0.4)	1	(0.1)
Movement disorder	1	(0.2)	0	(0.0)	1	(0.1)
Nervous system disorder	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**76**	**(14.3)**	**46**	**(17.3)**	**122**	**(15.3)**
Neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Neuritis cranial	1	(0.2)	1	(0.4)	2	(0.3)
Neuropathy peripheral	9	(1.7)	1	(0.4)	10	(1.3)
Optic neuritis	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	1	(0.2)	2	(0.8)	3	(0.4)
Polyneuropathy	2	(0.4)	2	(0.8)	4	(0.5)
Post herpetic neuralgia	2	(0.4)	1	(0.4)	3	(0.4)
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Restless legs syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Sciatica	2	(0.4)	1	(0.4)	3	(0.4)
Seizure	0	(0.0)	2	(0.8)	2	(0.3)
Senile dementia	0	(0.0)	1	(0.4)	1	(0.1)
Subarachnoid haemorrhage	0	(0.0)	1	(0.4)	1	(0.1)
Tension headache	2	(0.4)	1	(0.4)	3	(0.4)
Transient ischaemic attack	0	(0.0)	1	(0.4)	1	(0.1)
Tremor	1	(0.2)	1	(0.4)	2	(0.3)
VIIth nerve paralysis	7	(1.3)	0	(0.0)	7	(0.9)
Pregnancy, puerperium and perinatal conditions	**7**	**(1.3)**	**3**	**(1.1)**	**10**	**(1.3)**
Abortion	1	(0.2)	1	(0.4)	2	(0.3)
Abortion spontaneous	3	(0.6)	0	(0.0)	3	(0.4)
Ectopic pregnancy	2	(0.4)	0	(0.0)	2	(0.3)
Pregnancy	1	(0.2)	2	(0.8)	3	(0.4)
Psychiatric disorders	**113**	**(21.3)**	**71**	**(26.7)**	**184**	**(23.1)**
Adjustment disorder	1	(0.2)	0	(0.0)	1	(0.1)
Adjustment disorder with depressed mood	0	(0.0)	1	(0.4)	1	(0.1)
Affective disorder	1	(0.2)	1	(0.4)	2	(0.3)
Agoraphobia	1	(0.2)	0	(0.0)	1	(0.1)
Alcohol abuse	3	(0.6)	1	(0.4)	4	(0.5)
Alcoholism	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	39	(7.3)	18	(6.8)	57	(7.2)
Anxiety disorder	2	(0.4)	2	(0.8)	4	(0.5)
Attention deficit/hyperactivity disorder	8	(1.5)	5	(1.9)	13	(1.6)
Bipolar I disorder	1	(0.2)	0	(0.0)	1	(0.1)
Bipolar disorder	9	(1.7)	2	(0.8)	11	(1.4)
Bulimia nervosa	0	(0.0)	1	(0.4)	1	(0.1)
Depressed mood	3	(0.6)	0	(0.0)	3	(0.4)
Depression	46	(8.7)	32	(12.0)	78	(9.8)
Distractibility	1	(0.2)	0	(0.0)	1	(0.1)
Drug abuse	4	(0.8)	3	(1.1)	7	(0.9)
Drug dependence	4	(0.8)	1	(0.4)	5	(0.6)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**113**	**(21.3)**	**71**	**(26.7)**	**184**	**(23.1)**
Initial insomnia	4	(0.8)	1	(0.4)	5	(0.6)
Insomnia	18	(3.4)	10	(3.8)	28	(3.5)
Major depression	1	(0.2)	0	(0.0)	1	(0.1)
Mental disorder	1	(0.2)	1	(0.4)	2	(0.3)
Middle insomnia	2	(0.4)	1	(0.4)	3	(0.4)
Mood swings	1	(0.2)	0	(0.0)	1	(0.1)
Nicotine dependence	1	(0.2)	0	(0.0)	1	(0.1)
Nightmare	1	(0.2)	0	(0.0)	1	(0.1)
Obsessive-compulsive disorder	0	(0.0)	1	(0.4)	1	(0.1)
Panic attack	1	(0.2)	3	(1.1)	4	(0.5)
Personality disorder	1	(0.2)	1	(0.4)	2	(0.3)
Phobia	1	(0.2)	0	(0.0)	1	(0.1)
Post-traumatic stress disorder	3	(0.6)	1	(0.4)	4	(0.5)
Psychotic disorder	0	(0.0)	1	(0.4)	1	(0.1)
Restlessness	0	(0.0)	1	(0.4)	1	(0.1)
Schizophrenia, paranoid type	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	1	(0.2)	3	(1.1)	4	(0.5)
Social phobia	1	(0.2)	0	(0.0)	1	(0.1)
Somnambulism	1	(0.2)	0	(0.0)	1	(0.1)
Stress	0	(0.0)	2	(0.8)	2	(0.3)
Substance abuse	0	(0.0)	1	(0.4)	1	(0.1)
Tobacco abuse	11	(2.1)	8	(3.0)	19	(2.4)
Renal and urinary disorders	**22**	**(4.1)**	**12**	**(4.5)**	**34**	**(4.3)**
Acute kidney injury	1	(0.2)	0	(0.0)	1	(0.1)
Calculus urinary	2	(0.4)	0	(0.0)	2	(0.3)
Diabetic nephropathy	1	(0.2)	0	(0.0)	1	(0.1)
Dysuria	1	(0.2)	2	(0.8)	3	(0.4)
Haematuria	1	(0.2)	2	(0.8)	3	(0.4)
Microalbuminuria	1	(0.2)	1	(0.4)	2	(0.3)
Nephrolithiasis	9	(1.7)	4	(1.5)	13	(1.6)
Nephroptosis	0	(0.0)	1	(0.4)	1	(0.1)
Nocturia	1	(0.2)	0	(0.0)	1	(0.1)
Pollakiuria	0	(0.0)	1	(0.4)	1	(0.1)
Proteinuria	0	(0.0)	2	(0.8)	2	(0.3)
Renal atrophy	1	(0.2)	0	(0.0)	1	(0.1)
Renal cyst	1	(0.2)	1	(0.4)	2	(0.3)
Renal failure	1	(0.2)	0	(0.0)	1	(0.1)
Renal pain	1	(0.2)	0	(0.0)	1	(0.1)
Urethral discharge	1	(0.2)	0	(0.0)	1	(0.1)
Urinary hesitation	0	(0.0)	1	(0.4)	1	(0.1)
Urinary tract disorder	1	(0.2)	0	(0.0)	1	(0.1)
Urine abnormality	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**34**	**(6.4)**	**23**	**(8.6)**	**57**	**(7.2)**
Amenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	5	(0.9)	2	(0.8)	7	(0.9)
Breast mass	1	(0.2)	0	(0.0)	1	(0.1)
Breast pain	0	(0.0)	1	(0.4)	1	(0.1)
Calculus prostatic	1	(0.2)	0	(0.0)	1	(0.1)
Cervical dysplasia	3	(0.6)	1	(0.4)	4	(0.5)
Dysmenorrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Endometriosis	1	(0.2)	0	(0.0)	1	(0.1)
Erectile dysfunction	6	(1.1)	11	(4.1)	17	(2.1)
Fibrocystic breast disease	0	(0.0)	1	(0.4)	1	(0.1)
Genital ulceration	2	(0.4)	0	(0.0)	2	(0.3)
Gynaecomastia	1	(0.2)	3	(1.1)	4	(0.5)
Haematospermia	1	(0.2)	0	(0.0)	1	(0.1)
Menorrhagia	2	(0.4)	0	(0.0)	2	(0.3)
Menstruation irregular	1	(0.2)	0	(0.0)	1	(0.1)
Orchitis noninfective	0	(0.0)	1	(0.4)	1	(0.1)
Ovarian cyst	0	(0.0)	2	(0.8)	2	(0.3)
Pelvic pain	0	(0.0)	1	(0.4)	1	(0.1)
Penile discharge	2	(0.4)	0	(0.0)	2	(0.3)
Penis disorder	1	(0.2)	0	(0.0)	1	(0.1)
Polycystic ovaries	1	(0.2)	0	(0.0)	1	(0.1)
Prostatitis	1	(0.2)	0	(0.0)	1	(0.1)
Scrotal mass	1	(0.2)	0	(0.0)	1	(0.1)
Sexual dysfunction	1	(0.2)	0	(0.0)	1	(0.1)
Testicular atrophy	0	(0.0)	1	(0.4)	1	(0.1)
Testicular torsion	0	(0.0)	1	(0.4)	1	(0.1)
Uterine cyst	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal lesion	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele	2	(0.4)	0	(0.0)	2	(0.3)
Respiratory, thoracic and mediastinal disorders	**70**	**(13.2)**	**43**	**(16.2)**	**113**	**(14.2)**
Allergic sinusitis	3	(0.6)	0	(0.0)	3	(0.4)
Asthma	18	(3.4)	13	(4.9)	31	(3.9)
Asthma exercise induced	0	(0.0)	1	(0.4)	1	(0.1)
Bronchial hyperreactivity	0	(0.0)	1	(0.4)	1	(0.1)
Bronchitis chronic	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	1	(0.2)	1	(0.4)	2	(0.3)
Cough	7	(1.3)	5	(1.9)	12	(1.5)
Dysphonia	0	(0.0)	1	(0.4)	1	(0.1)
Dyspnoea	2	(0.4)	0	(0.0)	2	(0.3)
Dyspnoea exertional	1	(0.2)	0	(0.0)	1	(0.1)
Emphysema	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**70**	**(13.2)**	**43**	**(16.2)**	**113**	**(14.2)**
Haemoptysis	0	(0.0)	1	(0.4)	1	(0.1)
Hyperventilation	2	(0.4)	0	(0.0)	2	(0.3)
Laryngeal oedema	1	(0.2)	0	(0.0)	1	(0.1)
Nasal congestion	0	(0.0)	2	(0.8)	2	(0.3)
Nasal polyps	1	(0.2)	0	(0.0)	1	(0.1)
Nasal septum deviation	0	(0.0)	3	(1.1)	3	(0.4)
Nasal turbinate hypertrophy	1	(0.2)	1	(0.4)	2	(0.3)
Oropharyngeal pain	3	(0.6)	1	(0.4)	4	(0.5)
Pharyngeal inflammation	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax	1	(0.2)	0	(0.0)	1	(0.1)
Pneumothorax spontaneous	0	(0.0)	1	(0.4)	1	(0.1)
Pulmonary granuloma	1	(0.2)	0	(0.0)	1	(0.1)
Pulmonary oedema	1	(0.2)	0	(0.0)	1	(0.1)
Rhinitis allergic	18	(3.4)	9	(3.4)	27	(3.4)
Rhinorrhoea	0	(0.0)	1	(0.4)	1	(0.1)
Sinus congestion	2	(0.4)	3	(1.1)	5	(0.6)
Sinus disorder	1	(0.2)	0	(0.0)	1	(0.1)
Sleep apnoea syndrome	9	(1.7)	3	(1.1)	12	(1.5)
Tonsillar hypertrophy	7	(1.3)	3	(1.1)	10	(1.3)
Tonsillolith	0	(0.0)	1	(0.4)	1	(0.1)
Skin and subcutaneous tissue disorders	**102**	**(19.2)**	**51**	**(19.2)**	**153**	**(19.2)**
Acne	12	(2.3)	5	(1.9)	17	(2.1)
Actinic keratosis	0	(0.0)	1	(0.4)	1	(0.1)
Alopecia	4	(0.8)	5	(1.9)	9	(1.1)
Androgenetic alopecia	2	(0.4)	1	(0.4)	3	(0.4)
Angioedema	2	(0.4)	0	(0.0)	2	(0.3)
Blister	1	(0.2)	0	(0.0)	1	(0.1)
Dermal cyst	1	(0.2)	2	(0.8)	3	(0.4)
Dermatitis	6	(1.1)	4	(1.5)	10	(1.3)
Dermatitis acneiform	2	(0.4)	0	(0.0)	2	(0.3)
Dermatitis allergic	4	(0.8)	0	(0.0)	4	(0.5)
Dermatitis atopic	2	(0.4)	3	(1.1)	5	(0.6)
Dermatitis contact	5	(0.9)	3	(1.1)	8	(1.0)
Dry skin	2	(0.4)	5	(1.9)	7	(0.9)
Dyshidrotic eczema	3	(0.6)	0	(0.0)	3	(0.4)
Eczema	5	(0.9)	8	(3.0)	13	(1.6)
Eosinophilic pustular folliculitis	0	(0.0)	1	(0.4)	1	(0.1)
Erythema	2	(0.4)	0	(0.0)	2	(0.3)
Hyperhidrosis	2	(0.4)	0	(0.0)	2	(0.3)
Hyperkeratosis	1	(0.2)	0	(0.0)	1	(0.1)
Ingrowing nail	1	(0.2)	0	(0.0)	1	(0.1)
Ingrown hair	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**102**	**(19.2)**	**51**	**(19.2)**	**153**	**(19.2)**
Intertrigo	2	(0.4)	0	(0.0)	2	(0.3)
Keloid scar	1	(0.2)	0	(0.0)	1	(0.1)
Keratosis pilaris	0	(0.0)	1	(0.4)	1	(0.1)
Leukoplakia	0	(0.0)	1	(0.4)	1	(0.1)
Lipodystrophy acquired	1	(0.2)	0	(0.0)	1	(0.1)
Macule	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	2	(0.4)	0	(0.0)	2	(0.3)
Night sweats	8	(1.5)	4	(1.5)	12	(1.5)
Onycholysis	0	(0.0)	1	(0.4)	1	(0.1)
Papule	1	(0.2)	2	(0.8)	3	(0.4)
Photosensitivity reaction	1	(0.2)	0	(0.0)	1	(0.1)
Pityriasis rosea	1	(0.2)	0	(0.0)	1	(0.1)
Prurigo	0	(0.0)	1	(0.4)	1	(0.1)
Pruritus	4	(0.8)	2	(0.8)	6	(0.8)
Pruritus generalised	0	(0.0)	1	(0.4)	1	(0.1)
Psoriasis	6	(1.1)	3	(1.1)	9	(1.1)
Rash	14	(2.6)	4	(1.5)	18	(2.3)
Rash erythematous	1	(0.2)	0	(0.0)	1	(0.1)
Rash generalised	2	(0.4)	1	(0.4)	3	(0.4)
Rash maculo-papular	1	(0.2)	2	(0.8)	3	(0.4)
Rash papular	3	(0.6)	3	(1.1)	6	(0.8)
Rash pruritic	4	(0.8)	3	(1.1)	7	(0.9)
Rosacea	3	(0.6)	1	(0.4)	4	(0.5)
Sebaceous hyperplasia	0	(0.0)	1	(0.4)	1	(0.1)
Seborrhoeic dermatitis	8	(1.5)	3	(1.1)	11	(1.4)
Skin discolouration	0	(0.0)	1	(0.4)	1	(0.1)
Skin exfoliation	0	(0.0)	1	(0.4)	1	(0.1)
Skin fissures	1	(0.2)	0	(0.0)	1	(0.1)
Skin hyperpigmentation	0	(0.0)	1	(0.4)	1	(0.1)
Skin hypopigmentation	0	(0.0)	1	(0.4)	1	(0.1)
Skin lesion	1	(0.2)	1	(0.4)	2	(0.3)
Skin mass	1	(0.2)	0	(0.0)	1	(0.1)
Skin plaque	0	(0.0)	1	(0.4)	1	(0.1)
Skin striae	0	(0.0)	1	(0.4)	1	(0.1)
Skin ulcer	2	(0.4)	0	(0.0)	2	(0.3)
Solar dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	3	(0.6)	1	(0.4)	4	(0.5)
Urticaria chronic	0	(0.0)	1	(0.4)	1	(0.1)
Vitiligo	2	(0.4)	2	(0.8)	4	(0.5)
Social circumstances	**22**	**(4.1)**	**22**	**(8.3)**	**44**	**(5.5)**
Aborted pregnancy	2	(0.4)	0	(0.0)	2	(0.3)
Alcohol use	1	(0.2)	0	(0.0)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Social circumstances	**22**	**(4.1)**	**22**	**(8.3)**	**44**	**(5.5)**
Corrective lens user	3	(0.6)	5	(1.9)	8	(1.0)
Denture wearer	0	(0.0)	1	(0.4)	1	(0.1)
Drug abuser	1	(0.2)	0	(0.0)	1	(0.1)
Ex-drug abuser	1	(0.2)	0	(0.0)	1	(0.1)
Ex-tobacco user	2	(0.4)	0	(0.0)	2	(0.3)
Menopause	1	(0.2)	0	(0.0)	1	(0.1)
Poor personal hygiene	1	(0.2)	0	(0.0)	1	(0.1)
Postmenopause	1	(0.2)	1	(0.4)	2	(0.3)
Social alcohol drinker	0	(0.0)	1	(0.4)	1	(0.1)
Substance use	2	(0.4)	2	(0.8)	4	(0.5)
Tobacco user	12	(2.3)	12	(4.5)	24	(3.0)
Surgical and medical procedures	**78**	**(14.7)**	**33**	**(12.4)**	**111**	**(13.9)**
Abortion induced	1	(0.2)	0	(0.0)	1	(0.1)
Abscess drainage	1	(0.2)	1	(0.4)	2	(0.3)
Adenoidectomy	1	(0.2)	0	(0.0)	1	(0.1)
Anal fistula excision	0	(0.0)	2	(0.8)	2	(0.3)
Appendicectomy	12	(2.3)	7	(2.6)	19	(2.4)
Arterial stent insertion	1	(0.2)	0	(0.0)	1	(0.1)
Botulinum toxin injection	0	(0.0)	1	(0.4)	1	(0.1)
Breast prosthesis implantation	0	(0.0)	1	(0.4)	1	(0.1)
Caesarean section	1	(0.2)	0	(0.0)	1	(0.1)
Cancer surgery	0	(0.0)	1	(0.4)	1	(0.1)
Cardiac operation	0	(0.0)	1	(0.4)	1	(0.1)
Cardiac pacemaker insertion	1	(0.2)	0	(0.0)	1	(0.1)
Cervical conisation	1	(0.2)	0	(0.0)	1	(0.1)
Cholecystectomy	1	(0.2)	0	(0.0)	1	(0.1)
Circumcision	3	(0.6)	1	(0.4)	4	(0.5)
Colostomy	1	(0.2)	0	(0.0)	1	(0.1)
Colostomy closure	1	(0.2)	0	(0.0)	1	(0.1)
Coronary artery bypass	2	(0.4)	0	(0.0)	2	(0.3)
Curetting of chalazion	1	(0.2)	0	(0.0)	1	(0.1)
Cyst removal	2	(0.4)	1	(0.4)	3	(0.4)
Dental implantation	0	(0.0)	1	(0.4)	1	(0.1)
Diphtheria immunisation	0	(0.0)	1	(0.4)	1	(0.1)
Electrocoagulation	1	(0.2)	0	(0.0)	1	(0.1)
Eye laser surgery	1	(0.2)	0	(0.0)	1	(0.1)
Eye operation	1	(0.2)	0	(0.0)	1	(0.1)
Female sterilisation	6	(1.1)	1	(0.4)	7	(0.9)
Fracture treatment	1	(0.2)	0	(0.0)	1	(0.1)
Gastrectomy	2	(0.4)	0	(0.0)	2	(0.3)
Haemophilus influenzae type b immunisation	0	(0.0)	1	(0.4)	1	(0.1)
Haemorrhoid operation	2	(0.4)	1	(0.4)	3	(0.4)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Surgical and medical procedures	**78**	**(14.7)**	**33**	**(12.4)**	**111**	**(13.9)**
Hair transplant	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis A immunisation	1	(0.2)	1	(0.4)	2	(0.3)
Hepatitis B immunisation	2	(0.4)	1	(0.4)	3	(0.4)
Hernia repair	1	(0.2)	0	(0.0)	1	(0.1)
Hip arthroplasty	1	(0.2)	0	(0.0)	1	(0.1)
Hip surgery	0	(0.0)	1	(0.4)	1	(0.1)
Hysterectomy	5	(0.9)	0	(0.0)	5	(0.6)
Ileostomy	1	(0.2)	0	(0.0)	1	(0.1)
Influenza immunisation	2	(0.4)	0	(0.0)	2	(0.3)
Inguinal hernia repair	5	(0.9)	2	(0.8)	7	(0.9)
Intervertebral disc operation	0	(0.0)	1	(0.4)	1	(0.1)
Jaw operation	1	(0.2)	0	(0.0)	1	(0.1)
Joint fluid drainage	1	(0.2)	0	(0.0)	1	(0.1)
Laryngeal operation	1	(0.2)	0	(0.0)	1	(0.1)
Ligament operation	0	(0.0)	1	(0.4)	1	(0.1)
Limb operation	1	(0.2)	0	(0.0)	1	(0.1)
Lipectomy	1	(0.2)	0	(0.0)	1	(0.1)
Lipoinjection	1	(0.2)	0	(0.0)	1	(0.1)
Lipoma excision	2	(0.4)	0	(0.0)	2	(0.3)
Liposuction	3	(0.6)	0	(0.0)	3	(0.4)
Male genital tract operation	1	(0.2)	0	(0.0)	1	(0.1)
Meningococcal immunisation	2	(0.4)	0	(0.0)	2	(0.3)
Meniscus operation	1	(0.2)	0	(0.0)	1	(0.1)
Myomectomy	1	(0.2)	0	(0.0)	1	(0.1)
Nasal operation	1	(0.2)	0	(0.0)	1	(0.1)
Nasal septal operation	2	(0.4)	1	(0.4)	3	(0.4)
Neck surgery	1	(0.2)	0	(0.0)	1	(0.1)
Oophorectomy	1	(0.2)	0	(0.0)	1	(0.1)
Optic nerve operation	0	(0.0)	1	(0.4)	1	(0.1)
Osteosynthesis	1	(0.2)	0	(0.0)	1	(0.1)
Osteotomy	1	(0.2)	0	(0.0)	1	(0.1)
Otoplasty	1	(0.2)	0	(0.0)	1	(0.1)
Ovarian cystectomy	0	(0.0)	1	(0.4)	1	(0.1)
Ovarian operation	1	(0.2)	0	(0.0)	1	(0.1)
Papilloma excision	1	(0.2)	1	(0.4)	2	(0.3)
Pertussis immunisation	1	(0.2)	1	(0.4)	2	(0.3)
Phlebectomy	2	(0.4)	0	(0.0)	2	(0.3)
Pneumococcal immunisation	1	(0.2)	0	(0.0)	1	(0.1)
Polio immunisation	0	(0.0)	1	(0.4)	1	(0.1)
Polypectomy	2	(0.4)	0	(0.0)	2	(0.3)
Prophylaxis against gastrointestinal ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Prosthesis implantation	1	(0.2)	0	(0.0)	1	(0.1)
Pterygium operation	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Surgical and medical procedures	**78**	**(14.7)**	**33**	**(12.4)**	**111**	**(13.9)**
Ptosis repair	1	(0.2)	0	(0.0)	1	(0.1)
Rhinoplasty	3	(0.6)	3	(1.1)	6	(0.8)
Rotator cuff repair	1	(0.2)	0	(0.0)	1	(0.1)
Salpingo-oophorectomy	0	(0.0)	1	(0.4)	1	(0.1)
Sarcoma excision	0	(0.0)	1	(0.4)	1	(0.1)
Skin cosmetic procedure	1	(0.2)	0	(0.0)	1	(0.1)
Skin graft	1	(0.2)	0	(0.0)	1	(0.1)
Skin neoplasm excision	2	(0.4)	0	(0.0)	2	(0.3)
Splenectomy	1	(0.2)	0	(0.0)	1	(0.1)
Stent placement	0	(0.0)	1	(0.4)	1	(0.1)
Sterilisation	2	(0.4)	0	(0.0)	2	(0.3)
Stoma closure	1	(0.2)	0	(0.0)	1	(0.1)
Surgery	1	(0.2)	0	(0.0)	1	(0.1)
Tendon operation	1	(0.2)	0	(0.0)	1	(0.1)
Tendon sheath lesion excision	0	(0.0)	1	(0.4)	1	(0.1)
Testes exploration	1	(0.2)	0	(0.0)	1	(0.1)
Tetanus immunisation	1	(0.2)	1	(0.4)	2	(0.3)
Tonsillectomy	9	(1.7)	3	(1.1)	12	(1.5)
Turbinectomy	1	(0.2)	1	(0.4)	2	(0.3)
Umbilical hernia repair	3	(0.6)	0	(0.0)	3	(0.4)
Uterine cystectomy	1	(0.2)	0	(0.0)	1	(0.1)
Uterine dilation and curettage	1	(0.2)	0	(0.0)	1	(0.1)
Varicocele repair	1	(0.2)	0	(0.0)	1	(0.1)
Varicose vein operation	0	(0.0)	1	(0.4)	1	(0.1)
Vocal cord polypectomy	1	(0.2)	0	(0.0)	1	(0.1)
Wisdom teeth removal	0	(0.0)	1	(0.4)	1	(0.1)
Vascular disorders	**59**	**(11.1)**	**27**	**(10.2)**	**86**	**(10.8)**
Aortic arteriosclerosis	1	(0.2)	0	(0.0)	1	(0.1)
Arteriosclerosis	0	(0.0)	1	(0.4)	1	(0.1)
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Diastolic hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Essential hypertension	2	(0.4)	1	(0.4)	3	(0.4)
Hot flush	2	(0.4)	0	(0.0)	2	(0.3)
Hypertension	47	(8.9)	22	(8.3)	69	(8.7)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Lymphoedema	1	(0.2)	0	(0.0)	1	(0.1)
Microangiopathy	0	(0.0)	1	(0.4)	1	(0.1)
Peripheral arterial occlusive disease	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral vascular disorder	0	(0.0)	1	(0.4)	1	(0.1)
Peripheral venous disease	1	(0.2)	0	(0.0)	1	(0.1)
Post thrombotic syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Raynaud's phenomenon	0	(0.0)	1	(0.4)	1	(0.1)

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**59**	**(11.1)**	**27**	**(10.2)**	**86**	**(10.8)**
Thrombophlebitis	2	(0.4)	0	(0.0)	2	(0.3)
Varicose vein	3	(0.6)	2	(0.8)	5	(0.6)

Every subject is counted a single time for each applicable specific condition. A subject with multiple conditions within a system organ class is counted a single time for that system organ class.

A system organ class or specific condition appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 8

Subject Medical History Conditions
(Incidence >0% in One or More Treatment Groups)
AIDS Defining Condition

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
With one or more conditions	11	(2.1)	7	(2.6)	18	(2.3)
With no conditions	520	(97.9)	259	(97.4)	779	(97.7)
Infections and infestations	**11**	**(2.1)**	**6**	**(2.3)**	**17**	**(2.1)**
AIDS dementia complex	1	(0.2)	0	(0.0)	1	(0.1)
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)	1	(0.1)
Cryptococcosis	0	(0.0)	1	(0.4)	1	(0.1)
HIV wasting syndrome	2	(0.4)	1	(0.4)	3	(0.4)
Mycobacterium avium complex infection	0	(0.0)	1	(0.4)	1	(0.1)
Oesophageal candidiasis	1	(0.2)	3	(1.1)	4	(0.5)
Pneumocystis jirovecii pneumonia	5	(0.9)	2	(0.8)	7	(0.9)
Pneumonia	1	(0.2)	0	(0.0)	1	(0.1)
Tuberculosis	2	(0.4)	0	(0.0)	2	(0.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Kaposi's sarcoma AIDS related	0	(0.0)	1	(0.4)	1	(0.1)

Every subject is counted a single time for each applicable specific condition. A subject with multiple conditions within a system organ class is counted a single time for that system organ class.

A system organ class or specific condition appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 9

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
With one or more prior medications	308	(58.0)	180	(67.7)	488	(61.2)
With no prior medication	223	(42.0)	86	(32.3)	309	(38.8)
alimentary tract and metabolism						
anabolic agents for systemic use	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
stanozolol	0	(0.0)	1	(0.4)	1	(0.1)
antidiarrheals, intestinal antiinflammatory/antiinfective agents	**10**	**(1.9)**	**10**	**(3.8)**	**20**	**(2.5)**
Bifidobacterium animalis (+) Lactobacillus acidophilus	0	(0.0)	1	(0.4)	1	(0.1)
Enterococcus faecium	1	(0.2)	0	(0.0)	1	(0.1)
Lactobacillus acidophilus	2	(0.4)	0	(0.0)	2	(0.3)
Lactobacillus acidophilus (+) Lactobacillus rhamnosus	1	(0.2)	0	(0.0)	1	(0.1)
Lactobacillus rhamnosus (+) Saccharomyces boulardii	1	(0.2)	0	(0.0)	1	(0.1)
loperamide	0	(0.0)	1	(0.4)	1	(0.1)
loperamide hydrochloride	0	(0.0)	4	(1.5)	4	(0.5)
mesalamine	1	(0.2)	3	(1.1)	4	(0.5)
probiotics (unspecified)	2	(0.4)	1	(0.4)	3	(0.4)
smectite	2	(0.4)	0	(0.0)	2	(0.3)
antiemetics and antinauseants	**2**	**(0.4)**	**2**	**(0.8)**	**4**	**(0.5)**
dronabinol	1	(0.2)	0	(0.0)	1	(0.1)
ondansetron	1	(0.2)	0	(0.0)	1	(0.1)
ondansetron hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
drugs for acid related disorders	**27**	**(5.1)**	**26**	**(9.8)**	**53**	**(6.6)**
aluminum hydroxide (+) magnesium hydroxide (+) simethicone	1	(0.2)	0	(0.0)	1	(0.1)
calcium carbonate	1	(0.2)	2	(0.8)	3	(0.4)
calcium carbonate (+) sodium alginate (+) sodium bicarbonate	1	(0.2)	0	(0.0)	1	(0.1)
dexlansoprazole	0	(0.0)	2	(0.8)	2	(0.3)
esomeprazole	1	(0.2)	1	(0.4)	2	(0.3)
esomeprazole magnesium	3	(0.6)	3	(1.1)	6	(0.8)
famotidine	0	(0.0)	1	(0.4)	1	(0.1)
lansoprazole	1	(0.2)	2	(0.8)	3	(0.4)
magaldrate	1	(0.2)	0	(0.0)	1	(0.1)
misoprostol	0	(0.0)	1	(0.4)	1	(0.1)
omeprazole	11	(2.1)	13	(4.9)	24	(3.0)
omeprazole (+) sodium bicarbonate	0	(0.0)	1	(0.4)	1	(0.1)
omeprazole magnesium	1	(0.2)	0	(0.0)	1	(0.1)
pantoprazole	2	(0.4)	0	(0.0)	2	(0.3)
pantoprazole sodium	2	(0.4)	0	(0.0)	2	(0.3)
ranitidine	2	(0.4)	1	(0.4)	3	(0.4)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
drugs for acid related disorders	**27**	**(5.1)**	**26**	**(9.8)**	**53**	**(6.6)**
ranitidine hydrochloride	2	(0.4)	1	(0.4)	3	(0.4)
drugs for constipation	**7**	**(1.3)**	**3**	**(1.1)**	**10**	**(1.3)**
docusate sodium	0	(0.0)	2	(0.8)	2	(0.3)
flaxseed	2	(0.4)	0	(0.0)	2	(0.3)
polyethylene glycol 3350	2	(0.4)	0	(0.0)	2	(0.3)
polyethylene glycol 3350 (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride	2	(0.4)	0	(0.0)	2	(0.3)
psyllium husk	2	(0.4)	1	(0.4)	3	(0.4)
sodium picosulfate	1	(0.2)	0	(0.0)	1	(0.1)
drugs for functional gastrointestinal disorders	**6**	**(1.1)**	**2**	**(0.8)**	**8**	**(1.0)**
butylscopolamine bromide	2	(0.4)	0	(0.0)	2	(0.3)
domperidone	0	(0.0)	1	(0.4)	1	(0.1)
metoclopramide	1	(0.2)	1	(0.4)	2	(0.3)
phloroglucinol	1	(0.2)	0	(0.0)	1	(0.1)
simethicone	1	(0.2)	0	(0.0)	1	(0.1)
trimebutine	1	(0.2)	0	(0.0)	1	(0.1)
drugs used in diabetes	**8**	**(1.5)**	**5**	**(1.9)**	**13**	**(1.6)**
glipizide	2	(0.4)	0	(0.0)	2	(0.3)
glyburide	2	(0.4)	1	(0.4)	3	(0.4)
insulin aspart (+) insulin aspart protamine	0	(0.0)	1	(0.4)	1	(0.1)
insulin detemir	0	(0.0)	1	(0.4)	1	(0.1)
insulin glargine	2	(0.4)	0	(0.0)	2	(0.3)
liraglutide	1	(0.2)	0	(0.0)	1	(0.1)
metformin	4	(0.8)	2	(0.8)	6	(0.8)
metformin hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
metformin hydrochloride (+) sitagliptin phosphate	2	(0.4)	0	(0.0)	2	(0.3)
sitagliptin	1	(0.2)	0	(0.0)	1	(0.1)
mineral supplements	**11**	**(2.1)**	**12**	**(4.5)**	**23**	**(2.9)**
calcium (unspecified)	2	(0.4)	1	(0.4)	3	(0.4)
calcium (unspecified) (+) magnesium (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
calcium (unspecified) (+) vitamin D (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
calcium citrate (+) chromic chloride (+) copper citrate (+) ferrous citrate (+) magnesium citrate (+) potassium citrate (+) sodium citrate (+) sodium molybdate (+) sodium selenite (+) zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)
magnesium (unspecified)	0	(0.0)	3	(1.1)	3	(0.4)
magnesium sulfate	1	(0.2)	1	(0.4)	2	(0.3)
potassium (unspecified)	1	(0.2)	1	(0.4)	2	(0.3)
potassium chloride	1	(0.2)	1	(0.4)	2	(0.3)
potassium gluconate	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
mineral supplements	**11**	**(2.1)**	**12**	**(4.5)**	**23**	**(2.9)**
selenium (unspecified)	2	(0.4)	2	(0.8)	4	(0.5)
zinc (unspecified)	5	(0.9)	2	(0.8)	7	(0.9)
zinc sulfate	1	(0.2)	0	(0.0)	1	(0.1)
other alimentary tract and metabolism products	**5**	**(0.9)**	**0**	**(0.0)**	**5**	**(0.6)**
ademetionine sulfate tosylate (+) cyanocobalamin (+) leucovorin calcium	1	(0.2)	0	(0.0)	1	(0.1)
glutamine	1	(0.2)	0	(0.0)	1	(0.1)
lysine	2	(0.4)	0	(0.0)	2	(0.3)
xanthophyll (+) zeaxanthin	1	(0.2)	0	(0.0)	1	(0.1)
stomatological preparations	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
aluminum hydroxide (+) ibuprofen (+) lidocaine (+) magnesium hydroxide	0	(0.0)	1	(0.4)	1	(0.1)
benzoin (+) boric acid (+) levomenthol (+) phenyl salicylate (+) thymol	0	(0.0)	1	(0.4)	1	(0.1)
chlorhexidine gluconate (+) tixocortol pivalate	1	(0.2)	0	(0.0)	1	(0.1)
vitamins	**79**	**(14.9)**	**44**	**(16.5)**	**123**	**(15.4)**
acetylcysteine (+) bilberry (+) bioflavonoids (+) broccoli (+) bromelains (+) choline (+) cinnamon (+) inositol (+) lycopene (+) minerals (+) olive (+) pomegranate (+) tea (+) thioctic acid (+) turmeric (+) ubidecarenone (+) vitamins (+) xanthophyll	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid	17	(3.2)	11	(4.1)	28	(3.5)
ascorbic acid (+) beta carotene (+) ergocalciferol (+) folic acid (+) vitamin B complex (+) vitamin E	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) bioflavonoids (+) calcium (+) chromium (+) copper (+) folic acid (+) iodine (+) iron (+) lysine (+) manganese (+) magnesium (+) selenium (+) vitamin A (+) vitamin B complex (+) vitamin D (+) zinc	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) calcium (unspecified) (+) chromium (unspecified) (+) folic acid (+) magnesium (unspecified) (+) manganese (unspecified) (+) potassium (unspecified) (+) thioctic acid (+) vitamin B complex (+) zinc (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) folic acid (+) vitamin B complex	1	(0.2)	0	(0.0)	1	(0.1)
biotin	1	(0.2)	1	(0.4)	2	(0.3)
cholecalciferol	12	(2.3)	6	(2.3)	18	(2.3)
cod liver oil	0	(0.0)	1	(0.4)	1	(0.1)
cyanocobalamin (+) pyridoxine (+) thiamine	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
vitamins	**79**	**(14.9)**	**44**	**(16.5)**	**123**	**(15.4)**
ergocalciferol	1	(0.2)	0	(0.0)	1	(0.1)
ginseng (unspecified) (+) minerals (unspecified) (+) vitamins (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
minerals (unspecified) (+) vitamins (unspecified)	1	(0.2)	1	(0.4)	2	(0.3)
pyridoxine	8	(1.5)	2	(0.8)	10	(1.3)
vitamin B (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
vitamin B complex	7	(1.3)	8	(3.0)	15	(1.9)
vitamin D (unspecified)	13	(2.4)	5	(1.9)	18	(2.3)
vitamin E	4	(0.8)	2	(0.8)	6	(0.8)
vitamins (unspecified)	36	(6.8)	18	(6.8)	54	(6.8)
antiinfectives for systemic use						
antibacterials for systemic use	**99**	**(18.6)**	**56**	**(21.1)**	**155**	**(19.4)**
amoxicillin	8	(1.5)	5	(1.9)	13	(1.6)
amoxicillin (+) clavulanate potassium	2	(0.4)	3	(1.1)	5	(0.6)
ampicillin sodium (+) sulbactam sodium	1	(0.2)	0	(0.0)	1	(0.1)
antimicrobial (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
azithromycin	18	(3.4)	11	(4.1)	29	(3.6)
cefazolin sodium	0	(0.0)	1	(0.4)	1	(0.1)
cefpodoxime proxetil	0	(0.0)	1	(0.4)	1	(0.1)
ceftazidime	1	(0.2)	0	(0.0)	1	(0.1)
ceftriaxone	9	(1.7)	2	(0.8)	11	(1.4)
ceftriaxone sodium	3	(0.6)	0	(0.0)	3	(0.4)
cefuroxime	0	(0.0)	2	(0.8)	2	(0.3)
cephalexin	2	(0.4)	0	(0.0)	2	(0.3)
ciprofloxacin	3	(0.6)	2	(0.8)	5	(0.6)
clarithromycin	2	(0.4)	1	(0.4)	3	(0.4)
clindamycin	2	(0.4)	1	(0.4)	3	(0.4)
clindamycin hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
clindamycin phosphate	1	(0.2)	0	(0.0)	1	(0.1)
doxycycline	10	(1.9)	3	(1.1)	13	(1.6)
erythromycin	0	(0.0)	1	(0.4)	1	(0.1)
floxacillin	1	(0.2)	1	(0.4)	2	(0.3)
fusidic acid	1	(0.2)	0	(0.0)	1	(0.1)
levofloxacin	5	(0.9)	0	(0.0)	5	(0.6)
metronidazole	9	(1.7)	3	(1.1)	12	(1.5)
moxifloxacin	1	(0.2)	1	(0.4)	2	(0.3)
ofloxacin	1	(0.2)	0	(0.0)	1	(0.1)
penicillin (unspecified)	3	(0.6)	0	(0.0)	3	(0.4)
penicillin G	1	(0.2)	0	(0.0)	1	(0.1)
penicillin G benzathine	10	(1.9)	6	(2.3)	16	(2.0)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiinfectives for systemic use						
antibacterials for systemic use	**99**	**(18.6)**	**56**	**(21.1)**	**155**	**(19.4)**
penicillin G benzathine (+) tolycaine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
penicillin V potassium	1	(0.2)	0	(0.0)	1	(0.1)
roxithromycin	1	(0.2)	0	(0.0)	1	(0.1)
sulfadiazine	0	(0.0)	1	(0.4)	1	(0.1)
sulfamethoxazole (+) trimethoprim	38	(7.2)	30	(11.3)	68	(8.5)
antimycobacterials	**10**	**(1.9)**	**7**	**(2.6)**	**17**	**(2.1)**
dapsone	0	(0.0)	1	(0.4)	1	(0.1)
ethambutol	1	(0.2)	0	(0.0)	1	(0.1)
isoniazid	9	(1.7)	6	(2.3)	15	(1.9)
antimycotics for systemic use	**11**	**(2.1)**	**9**	**(3.4)**	**20**	**(2.5)**
amphotericin B (+) cholesterol (+) distearoylphosphatidylglycerol (+) vitamin E	0	(0.0)	1	(0.4)	1	(0.1)
fluconazole	11	(2.1)	9	(3.4)	20	(2.5)
antivirals for systemic use	**21**	**(4.0)**	**16**	**(6.0)**	**37**	**(4.6)**
acyclovir	11	(2.1)	8	(3.0)	19	(2.4)
famciclovir	0	(0.0)	1	(0.4)	1	(0.1)
ganciclovir	1	(0.2)	0	(0.0)	1	(0.1)
valacyclovir hydrochloride	9	(1.7)	8	(3.0)	17	(2.1)
vaccines	**21**	**(4.0)**	**17**	**(6.4)**	**38**	**(4.8)**
HPV rL1 6 11 16 18 VLP vaccine (yeast)	2	(0.4)	1	(0.4)	3	(0.4)
diphtheria toxoid (+) pertussis acellular vaccine (unspecified) (+) tetanus toxoid	1	(0.2)	2	(0.8)	3	(0.4)
diphtheria toxoid (+) poliovirus vaccine inactivated (Vero) (+) tetanus toxoid	1	(0.2)	0	(0.0)	1	(0.1)
hepatitis A virus vaccine (unspecified)	2	(0.4)	1	(0.4)	3	(0.4)
hepatitis A virus vaccine inactivated (+) hepatitis B virus vaccine rHBsAg (yeast)	1	(0.2)	0	(0.0)	1	(0.1)
hepatitis B virus vaccine (unspecified)	5	(0.9)	4	(1.5)	9	(1.1)
hepatitis B virus vaccine rHBsAg (yeast)	3	(0.6)	0	(0.0)	3	(0.4)
influenza virus sAg 3v vaccine inactivated	3	(0.6)	1	(0.4)	4	(0.5)
influenza virus split virion 3v vaccine inactivated	3	(0.6)	2	(0.8)	5	(0.6)
influenza virus vaccine (unspecified)	6	(1.1)	9	(3.4)	15	(1.9)
pertussis vaccine (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
pneumococcal 13v conj vaccine (CRM197)	0	(0.0)	3	(1.1)	3	(0.4)
pneumococcal 23v polysaccharide vaccine	0	(0.0)	3	(1.1)	3	(0.4)
pneumococcal vaccine (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
antineoplastic and immunomodulating agents						
antineoplastic agents	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
fluorouracil	1	(0.2)	0	(0.0)	1	(0.1)
hydroxyurea	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiparasitic products, insecticides, and repellents						
antiprotozoals	**4**	**(0.8)**	**5**	**(1.9)**	**9**	**(1.1)**
atovaquone	3	(0.6)	3	(1.1)	6	(0.8)
nitazoxanide	1	(0.2)	0	(0.0)	1	(0.1)
pentamidine isethionate	0	(0.0)	2	(0.8)	2	(0.3)
pyrimethamine	0	(0.0)	2	(0.8)	2	(0.3)
blood and blood forming organs						
antianemic preparations	**8**	**(1.5)**	**7**	**(2.6)**	**15**	**(1.9)**
ascorbic acid (+) beta carotene (+) calcium carbonate (+) carbonyl iron (+) cholecalciferol (+) copper (unspecified) (+) docusate sodium (+) folic acid (+) magnesium oxide (+) vitamin B complex (+) vitamin E acetate (+) zinc oxide	0	(0.0)	1	(0.4)	1	(0.1)
cyanocobalamin	3	(0.6)	3	(1.1)	6	(0.8)
ferrous sulfate	2	(0.4)	3	(1.1)	5	(0.6)
folic acid	3	(0.6)	2	(0.8)	5	(0.6)
folic acid (+) iron polymaltose	1	(0.2)	0	(0.0)	1	(0.1)
iron (unspecified)	3	(0.6)	0	(0.0)	3	(0.4)
mecobalamin	1	(0.2)	0	(0.0)	1	(0.1)
antihemorrhagics	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
factor VIII	0	(0.0)	1	(0.4)	1	(0.1)
antithrombotic agents	**5**	**(0.9)**	**1**	**(0.4)**	**6**	**(0.8)**
clopidogrel	0	(0.0)	1	(0.4)	1	(0.1)
enoxaparin sodium	2	(0.4)	0	(0.0)	2	(0.3)
rivaroxaban	1	(0.2)	0	(0.0)	1	(0.1)
ticagrelor	1	(0.2)	0	(0.0)	1	(0.1)
warfarin sodium	1	(0.2)	0	(0.0)	1	(0.1)
blood substitutes and perfusion solutions	**0**	**(0.0)**	**4**	**(1.5)**	**4**	**(0.5)**
electrolytes (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
electrolytes (unspecified) (+) sodium lactate	0	(0.0)	1	(0.4)	1	(0.1)
sodium chloride	0	(0.0)	3	(1.1)	3	(0.4)
cardiovascular system						
agents acting on the renin-angiotensin system	**28**	**(5.3)**	**11**	**(4.1)**	**39**	**(4.9)**
amlodipine besylate (+) valsartan	1	(0.2)	0	(0.0)	1	(0.1)
benazepril hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
candesartan	0	(0.0)	1	(0.4)	1	(0.1)
candesartan cilexetil	2	(0.4)	0	(0.0)	2	(0.3)
candesartan cilexetil (+) hydrochlorothiazide	1	(0.2)	0	(0.0)	1	(0.1)
enalapril	5	(0.9)	1	(0.4)	6	(0.8)
hydrochlorothiazide (+) lisinopril	1	(0.2)	0	(0.0)	1	(0.1)
hydrochlorothiazide (+) olmesartan medoxomil	0	(0.0)	1	(0.4)	1	(0.1)
indapamide (+) perindopril erbumine	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
cardiovascular system						
agents acting on the renin-angiotensin system	**28**	**(5.3)**	**11**	**(4.1)**	**39**	**(4.9)**
lisinopril	10	(1.9)	2	(0.8)	12	(1.5)
losartan	1	(0.2)	3	(1.1)	4	(0.5)
losartan potassium	1	(0.2)	0	(0.0)	1	(0.1)
olmesartan medoxomil	1	(0.2)	0	(0.0)	1	(0.1)
perindopril erbumine	1	(0.2)	0	(0.0)	1	(0.1)
ramipril	2	(0.4)	2	(0.8)	4	(0.5)
valsartan	0	(0.0)	1	(0.4)	1	(0.1)
antihypertensives	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
clonidine	1	(0.2)	0	(0.0)	1	(0.1)
beta blocking agents	**10**	**(1.9)**	**7**	**(2.6)**	**17**	**(2.1)**
atenolol	1	(0.2)	1	(0.4)	2	(0.3)
bisoprolol	5	(0.9)	3	(1.1)	8	(1.0)
bisoprolol fumarate	1	(0.2)	0	(0.0)	1	(0.1)
carvedilol	2	(0.4)	1	(0.4)	3	(0.4)
metoprolol	1	(0.2)	1	(0.4)	2	(0.3)
propranolol hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
calcium channel blockers	**12**	**(2.3)**	**5**	**(1.9)**	**17**	**(2.1)**
amlodipine	6	(1.1)	3	(1.1)	9	(1.1)
amlodipine besylate	3	(0.6)	2	(0.8)	5	(0.6)
diltiazem	1	(0.2)	0	(0.0)	1	(0.1)
felodipine	0	(0.0)	1	(0.4)	1	(0.1)
nifedipine	2	(0.4)	0	(0.0)	2	(0.3)
cardiac therapy	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
dofetilide	1	(0.2)	0	(0.0)	1	(0.1)
ubidecarenone	0	(0.0)	1	(0.4)	1	(0.1)
ubiquinol	1	(0.2)	0	(0.0)	1	(0.1)
diuretics	**7**	**(1.3)**	**3**	**(1.1)**	**10**	**(1.3)**
hydrochlorothiazide	7	(1.3)	1	(0.4)	8	(1.0)
piretanide	0	(0.0)	1	(0.4)	1	(0.1)
torsemide	0	(0.0)	1	(0.4)	1	(0.1)
lipid modifying agents	**33**	**(6.2)**	**14**	**(5.3)**	**47**	**(5.9)**
atorvastatin	2	(0.4)	1	(0.4)	3	(0.4)
atorvastatin calcium	4	(0.8)	1	(0.4)	5	(0.6)
black currant seed oil (+) borage oil (+) evening primrose oil (+) flaxseed (+) omega-3 marine triglycerides	1	(0.2)	0	(0.0)	1	(0.1)
borage oil (+) flaxseed (+) omega-3 marine triglycerides (+) vitamin E	1	(0.2)	0	(0.0)	1	(0.1)
ciprofibrate	0	(0.0)	1	(0.4)	1	(0.1)
fenofibrate	3	(0.6)	0	(0.0)	3	(0.4)
icosapent ethyl	1	(0.2)	0	(0.0)	1	(0.1)
lovastatin	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
cardiovascular system						
lipid modifying agents	**33**	**(6.2)**	**14**	**(5.3)**	**47**	**(5.9)**
niacin	1	(0.2)	1	(0.4)	2	(0.3)
omega-3 acid ethyl esters	1	(0.2)	1	(0.4)	2	(0.3)
omega-3 marine triglycerides	13	(2.4)	4	(1.5)	17	(2.1)
pravastatin	1	(0.2)	1	(0.4)	2	(0.3)
rosuvastatin	3	(0.6)	0	(0.0)	3	(0.4)
rosuvastatin calcium	3	(0.6)	3	(1.1)	6	(0.8)
simvastatin	4	(0.8)	2	(0.8)	6	(0.8)
peripheral vasodilators	**0**	**(0.0)**	**2**	**(0.8)**	**2**	**(0.3)**
pentoxifylline	0	(0.0)	1	(0.4)	1	(0.1)
xanthinol niacinate	0	(0.0)	1	(0.4)	1	(0.1)
dermatologicals						
anti-acne preparations	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
isotretinoin	1	(0.2)	0	(0.0)	1	(0.1)
tretinoin	1	(0.2)	0	(0.0)	1	(0.1)
antibiotics and chemotherapeutics for dermatological use	**3**	**(0.6)**	**1**	**(0.4)**	**4**	**(0.5)**
bacitracin	0	(0.0)	1	(0.4)	1	(0.1)
imiquimod	3	(0.6)	0	(0.0)	3	(0.4)
podophyllum resin	1	(0.2)	0	(0.0)	1	(0.1)
antifungals for dermatological use	**21**	**(4.0)**	**9**	**(3.4)**	**30**	**(3.8)**
amorolfine	1	(0.2)	1	(0.4)	2	(0.3)
betamethasone valerate (+) clotrimazole (+) neomycin sulfate	1	(0.2)	0	(0.0)	1	(0.1)
ciclopirox	1	(0.2)	1	(0.4)	2	(0.3)
clotrimazole	3	(0.6)	1	(0.4)	4	(0.5)
econazole	1	(0.2)	1	(0.4)	2	(0.3)
flucytosine	0	(0.0)	1	(0.4)	1	(0.1)
ketoconazole	3	(0.6)	1	(0.4)	4	(0.5)
miconazole nitrate	1	(0.2)	1	(0.4)	2	(0.3)
nystatin	7	(1.3)	2	(0.8)	9	(1.1)
terbinafine	7	(1.3)	0	(0.0)	7	(0.9)
terbinafine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
corticosteroids, dermatological preparations	**11**	**(2.1)**	**8**	**(3.0)**	**19**	**(2.4)**
betamethasone dipropionate	1	(0.2)	0	(0.0)	1	(0.1)
betamethasone dipropionate (+) calcipotriene	1	(0.2)	0	(0.0)	1	(0.1)
betamethasone dipropionate (+) gentamicin sulfate	1	(0.2)	1	(0.4)	2	(0.3)
betamethasone valerate	0	(0.0)	1	(0.4)	1	(0.1)
betamethasone valerate (+) fusidic acid	0	(0.0)	1	(0.4)	1	(0.1)
chlorhexidine hydrochloride (+) dexamethasone (+) nystatin	1	(0.2)	0	(0.0)	1	(0.1)
clobetasol propionate	1	(0.2)	1	(0.4)	2	(0.3)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
dermatologicals						
corticosteroids, dermatological preparations	**11**	**(2.1)**	**8**	**(3.0)**	**19**	**(2.4)**
diflucortolone valerate	1	(0.2)	0	(0.0)	1	(0.1)
difluprednate	1	(0.2)	0	(0.0)	1	(0.1)
fluocinolone acetonide	0	(0.0)	1	(0.4)	1	(0.1)
fluorometholone	1	(0.2)	0	(0.0)	1	(0.1)
fluprednidene acetate (+) miconazole nitrate	1	(0.2)	0	(0.0)	1	(0.1)
hydrocortisone acetate	2	(0.4)	0	(0.0)	2	(0.3)
methylprednisolone aceponate	0	(0.0)	1	(0.4)	1	(0.1)
mometasone furoate	0	(0.0)	2	(0.8)	2	(0.3)
emollients and protectives	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
coconut oil	1	(0.2)	0	(0.0)	1	(0.1)
urea	1	(0.2)	0	(0.0)	1	(0.1)
other dermatological preparations	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**
ammonium lactate	1	(0.2)	1	(0.4)	2	(0.3)
chlorophyll	1	(0.2)	0	(0.0)	1	(0.1)
minoxidil	0	(0.0)	1	(0.4)	1	(0.1)
sodium phenolsulfonic acid phenol formaldehyde urea condensate	1	(0.2)	0	(0.0)	1	(0.1)
genitourinary system and sex hormones						
sex hormones and modulators of the genital system	**30**	**(5.6)**	**7**	**(2.6)**	**37**	**(4.6)**
chlormadinone acetate (+) ethinyl estradiol	0	(0.0)	1	(0.4)	1	(0.1)
cyproterone acetate (+) ethinyl estradiol	1	(0.2)	1	(0.4)	2	(0.3)
ethinyl estradiol (+) ferrous fumarate (+) norethindrone acetate	1	(0.2)	0	(0.0)	1	(0.1)
ethinyl estradiol (+) gestodene	2	(0.4)	0	(0.0)	2	(0.3)
ethinyl estradiol (+) levonorgestrel	1	(0.2)	0	(0.0)	1	(0.1)
ethinyl estradiol (+) norgestimate	1	(0.2)	0	(0.0)	1	(0.1)
ethynodiol diacetate (+) mestranol	1	(0.2)	0	(0.0)	1	(0.1)
levonorgestrel	2	(0.4)	0	(0.0)	2	(0.3)
medroxyprogesterone acetate	17	(3.2)	4	(1.5)	21	(2.6)
norethindrone enanthate	2	(0.4)	0	(0.0)	2	(0.3)
testosterone	1	(0.2)	1	(0.4)	2	(0.3)
testosterone cypionate	1	(0.2)	0	(0.0)	1	(0.1)
urologicals	**9**	**(1.7)**	**11**	**(4.1)**	**20**	**(2.5)**
alfuzosin hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
finasteride	3	(0.6)	4	(1.5)	7	(0.9)
sildenafil citrate	1	(0.2)	1	(0.4)	2	(0.3)
solifenacin succinate	0	(0.0)	1	(0.4)	1	(0.1)
tadalafil	3	(0.6)	3	(1.1)	6	(0.8)
tamsulosin hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
vardenafil hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
musculoskeletal system						
antigout preparations	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
allopurinol	2	(0.4)	1	(0.4)	3	(0.4)
antiinflammatory and antirheumatic products	**36**	**(6.8)**	**23**	**(8.6)**	**59**	**(7.4)**
benzydamine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
diclofenac	2	(0.4)	2	(0.8)	4	(0.5)
diclofenac diethylamine	0	(0.0)	1	(0.4)	1	(0.1)
diclofenac sodium	1	(0.2)	2	(0.8)	3	(0.4)
etodolac	1	(0.2)	0	(0.0)	1	(0.1)
etoricoxib	2	(0.4)	0	(0.0)	2	(0.3)
ibuprofen	18	(3.4)	16	(6.0)	34	(4.3)
ibuprofen lysine	1	(0.2)	0	(0.0)	1	(0.1)
indomethacin	0	(0.0)	1	(0.4)	1	(0.1)
ketoprofen	1	(0.2)	0	(0.0)	1	(0.1)
ketorolac tromethamine	1	(0.2)	0	(0.0)	1	(0.1)
mefenamic acid	2	(0.4)	0	(0.0)	2	(0.3)
meloxicam	1	(0.2)	1	(0.4)	2	(0.3)
nabumetone	1	(0.2)	0	(0.0)	1	(0.1)
naproxen	4	(0.8)	0	(0.0)	4	(0.5)
naproxen sodium	2	(0.4)	1	(0.4)	3	(0.4)
muscle relaxants	**7**	**(1.3)**	**0**	**(0.0)**	**7**	**(0.9)**
acetaminophen (+) caffeine (+) carisoprodol (+) diclofenac sodium	1	(0.2)	0	(0.0)	1	(0.1)
chlormezanone	1	(0.2)	0	(0.0)	1	(0.1)
cyclobenzaprine hydrochloride	4	(0.8)	0	(0.0)	4	(0.5)
methocarbamol	2	(0.4)	0	(0.0)	2	(0.3)
topical products for joint and muscular pain	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
menthol (+) methyl salicylate	1	(0.2)	0	(0.0)	1	(0.1)
nervous system						
analgesics	**55**	**(10.4)**	**30**	**(11.3)**	**85**	**(10.7)**
acetaminophen	26	(4.9)	12	(4.5)	38	(4.8)
acetaminophen (+) aspirin (+) caffeine	0	(0.0)	3	(1.1)	3	(0.4)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) phenylephrine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
acetaminophen (+) caffeine (+) codeine phosphate (+) doxylamine succinate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) cetirizine hydrochloride (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) chlorpheniramine maleate (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) codeine phosphate	1	(0.2)	2	(0.8)	3	(0.4)
acetaminophen (+) dextromethorphan hydrobromide (+) promethazine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
analgesics	**55**	**(10.4)**	**30**	**(11.3)**	**85**	**(10.7)**
acetaminophen (+) hydrocodone bitartrate	1	(0.2)	2	(0.8)	3	(0.4)
acetaminophen (+) oxycodone hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
acetaminophen (+) pholcodine (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) pseudoephedrine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
acetaminophen (+) tramadol hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
aspirin	13	(2.4)	4	(1.5)	17	(2.1)
aspirin lysine	1	(0.2)	0	(0.0)	1	(0.1)
buprenorphine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
dipyrone	4	(0.8)	2	(0.8)	6	(0.8)
eletriptan	0	(0.0)	1	(0.4)	1	(0.1)
eletriptan hydrobromide	0	(0.0)	1	(0.4)	1	(0.1)
fentanyl	1	(0.2)	1	(0.4)	2	(0.3)
hydromorphone hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
morphine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
morphine sulfate	1	(0.2)	0	(0.0)	1	(0.1)
oxycodone	0	(0.0)	1	(0.4)	1	(0.1)
oxycodone hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
pizotyline malate	1	(0.2)	0	(0.0)	1	(0.1)
tramadol hydrochloride	7	(1.3)	2	(0.8)	9	(1.1)
zolmitriptan	1	(0.2)	0	(0.0)	1	(0.1)
anesthetics	**1**	**(0.2)**	**4**	**(1.5)**	**5**	**(0.6)**
bupivacaine	0	(0.0)	1	(0.4)	1	(0.1)
lidocaine	1	(0.2)	3	(1.1)	4	(0.5)
propofol	0	(0.0)	1	(0.4)	1	(0.1)
anti-Parkinson drugs	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
biperiden hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
antiepileptics	**26**	**(4.9)**	**16**	**(6.0)**	**42**	**(5.3)**
carbamazepine	1	(0.2)	2	(0.8)	3	(0.4)
clonazepam	5	(0.9)	5	(1.9)	10	(1.3)
divalproex sodium	2	(0.4)	0	(0.0)	2	(0.3)
gabapentin	6	(1.1)	2	(0.8)	8	(1.0)
lamotrigine	1	(0.2)	2	(0.8)	3	(0.4)
levetiracetam	2	(0.4)	1	(0.4)	3	(0.4)
oxcarbazepine	0	(0.0)	1	(0.4)	1	(0.1)
pregabalin	7	(1.3)	3	(1.1)	10	(1.3)
primidone	1	(0.2)	0	(0.0)	1	(0.1)
topiramate	1	(0.2)	1	(0.4)	2	(0.3)
valproate sodium	2	(0.4)	2	(0.8)	4	(0.5)
valproic acid	1	(0.2)	0	(0.0)	1	(0.1)
other nervous system drugs	**5**	**(0.9)**	**2**	**(0.8)**	**7**	**(0.9)**
betahistine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
other nervous system drugs	**5**	**(0.9)**	**2**	**(0.8)**	**7**	**(0.9)**
buprenorphine hydrochloride (+) naloxone hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
methadone hydrochloride	4	(0.8)	0	(0.0)	4	(0.5)
nicotine	0	(0.0)	1	(0.4)	1	(0.1)
psychoanaleptics	**34**	**(6.4)**	**31**	**(11.7)**	**65**	**(8.2)**
Asian ginseng (+) deanol tartrate (+) minerals (unspecified) (+) rutin (+) vitamins (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
acetylcarnitine	1	(0.2)	0	(0.0)	1	(0.1)
amitriptyline hydrochloride	5	(0.9)	1	(0.4)	6	(0.8)
amphetamine aspartate (+) amphetamine sulfate (+) dextroamphetamine saccharate (+) dextroamphetamine sulfate	5	(0.9)	3	(1.1)	8	(1.0)
bupropion hydrochloride	2	(0.4)	4	(1.5)	6	(0.8)
citalopram	1	(0.2)	2	(0.8)	3	(0.4)
citalopram hydrobromide	2	(0.4)	2	(0.8)	4	(0.5)
dextroamphetamine sulfate	1	(0.2)	0	(0.0)	1	(0.1)
dothiepin hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
duloxetine hydrochloride	1	(0.2)	3	(1.1)	4	(0.5)
escitalopram	1	(0.2)	1	(0.4)	2	(0.3)
escitalopram oxalate	5	(0.9)	4	(1.5)	9	(1.1)
fluvoxamine maleate	0	(0.0)	1	(0.4)	1	(0.1)
memantine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
mephedrone	1	(0.2)	0	(0.0)	1	(0.1)
methamphetamine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
methylenedioxymethamphetamine	1	(0.2)	0	(0.0)	1	(0.1)
methylphenidate hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
mirtazapine	3	(0.6)	3	(1.1)	6	(0.8)
paroxetine	2	(0.4)	0	(0.0)	2	(0.3)
paroxetine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
sertraline hydrochloride	4	(0.8)	4	(1.5)	8	(1.0)
trazodone hydrochloride	5	(0.9)	3	(1.1)	8	(1.0)
venlafaxine hydrochloride	1	(0.2)	2	(0.8)	3	(0.4)
psycholeptics	**41**	**(7.7)**	**21**	**(7.9)**	**62**	**(7.8)**
alprazolam	10	(1.9)	5	(1.9)	15	(1.9)
aripiprazole	0	(0.0)	1	(0.4)	1	(0.1)
bromazepam	3	(0.6)	0	(0.0)	3	(0.4)
chlordiazepoxide	1	(0.2)	0	(0.0)	1	(0.1)
clobazam	1	(0.2)	0	(0.0)	1	(0.1)
cloxazolam	1	(0.2)	0	(0.0)	1	(0.1)
diazepam	4	(0.8)	2	(0.8)	6	(0.8)
ethyl loflazepate	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
psycholeptics	**41**	**(7.7)**	**21**	**(7.9)**	**62**	**(7.8)**
fluphenazine	1	(0.2)	0	(0.0)	1	(0.1)
haloperidol	1	(0.2)	1	(0.4)	2	(0.3)
hydroxyzine	1	(0.2)	0	(0.0)	1	(0.1)
hydroxyzine hydrochloride	3	(0.6)	0	(0.0)	3	(0.4)
lithium	1	(0.2)	0	(0.0)	1	(0.1)
lorazepam	8	(1.5)	6	(2.3)	14	(1.8)
lormetazepam	0	(0.0)	1	(0.4)	1	(0.1)
mebutamate	1	(0.2)	0	(0.0)	1	(0.1)
melatonin	1	(0.2)	1	(0.4)	2	(0.3)
olanzapine	0	(0.0)	1	(0.4)	1	(0.1)
passionflower (+) valerian	0	(0.0)	1	(0.4)	1	(0.1)
prochlorperazine edisylate	1	(0.2)	0	(0.0)	1	(0.1)
quetiapine fumarate	1	(0.2)	1	(0.4)	2	(0.3)
risperidone	1	(0.2)	0	(0.0)	1	(0.1)
sulpiride	0	(0.0)	1	(0.4)	1	(0.1)
temazepam	0	(0.0)	1	(0.4)	1	(0.1)
zolpidem	1	(0.2)	1	(0.4)	2	(0.3)
zolpidem tartrate	3	(0.6)	1	(0.4)	4	(0.5)
zopiclone	3	(0.6)	0	(0.0)	3	(0.4)
respiratory system						
antihistamines for systemic use	**26**	**(4.9)**	**11**	**(4.1)**	**37**	**(4.6)**
bilastine	0	(0.0)	1	(0.4)	1	(0.1)
cetirizine hydrochloride	9	(1.7)	5	(1.9)	14	(1.8)
chlorpheniramine	1	(0.2)	0	(0.0)	1	(0.1)
chlorpheniramine maleate	3	(0.6)	0	(0.0)	3	(0.4)
desloratadine	3	(0.6)	1	(0.4)	4	(0.5)
dimenhydrinate	0	(0.0)	2	(0.8)	2	(0.3)
diphenhydramine	0	(0.0)	1	(0.4)	1	(0.1)
diphenhydramine hydrochloride	4	(0.8)	0	(0.0)	4	(0.5)
fexofenadine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
ketotifen fumarate	1	(0.2)	0	(0.0)	1	(0.1)
levocetirizine dihydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
loratadine	4	(0.8)	2	(0.8)	6	(0.8)
promethazine	1	(0.2)	0	(0.0)	1	(0.1)
cough and cold preparations	**6**	**(1.1)**	**4**	**(1.5)**	**10**	**(1.3)**
Indian squill (+) ipecac (+) licorice	0	(0.0)	1	(0.4)	1	(0.1)
acetylcysteine	1	(0.2)	1	(0.4)	2	(0.3)
bromhexine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
carbocysteine	0	(0.0)	1	(0.4)	1	(0.1)
dextromethorphan hydrobromide (+) guaifenesin (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
respiratory system						
cough and cold preparations	**6**	**(1.1)**	**4**	**(1.5)**	**10**	**(1.3)**
dextromethorphan hydrobromide (+) lysozyme chloride (+) potassium cresolsulfonate	1	(0.2)	0	(0.0)	1	(0.1)
guaifenesin	1	(0.2)	0	(0.0)	1	(0.1)
guaifenesin (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
potassium iodide	1	(0.2)	0	(0.0)	1	(0.1)
drugs for obstructive airway diseases	**14**	**(2.6)**	**9**	**(3.4)**	**23**	**(2.9)**
aclidinium bromide	1	(0.2)	0	(0.0)	1	(0.1)
albuterol	8	(1.5)	1	(0.4)	9	(1.1)
albuterol sulfate	2	(0.4)	2	(0.8)	4	(0.5)
arformoterol tartrate	0	(0.0)	1	(0.4)	1	(0.1)
beclomethasone dipropionate	2	(0.4)	0	(0.0)	2	(0.3)
beclomethasone dipropionate (+) formoterol fumarate	1	(0.2)	0	(0.0)	1	(0.1)
budesonide	0	(0.0)	2	(0.8)	2	(0.3)
budesonide (+) formoterol fumarate	1	(0.2)	0	(0.0)	1	(0.1)
ciclesonide	1	(0.2)	0	(0.0)	1	(0.1)
epinephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
fenoterol hydrobromide (+) ipratropium bromide	1	(0.2)	0	(0.0)	1	(0.1)
fluticasone	1	(0.2)	0	(0.0)	1	(0.1)
fluticasone furoate	0	(0.0)	1	(0.4)	1	(0.1)
fluticasone propionate	1	(0.2)	2	(0.8)	3	(0.4)
fluticasone propionate (+) salmeterol xinafoate	1	(0.2)	2	(0.8)	3	(0.4)
montelukast	2	(0.4)	0	(0.0)	2	(0.3)
montelukast sodium	1	(0.2)	0	(0.0)	1	(0.1)
salmeterol	1	(0.2)	0	(0.0)	1	(0.1)
terbutaline sulfate	0	(0.0)	1	(0.4)	1	(0.1)
nasal preparations	**6**	**(1.1)**	**6**	**(2.3)**	**12**	**(1.5)**
framycetin sulfate (+) naphazoline nitrate (+) prednisolone acetate	0	(0.0)	1	(0.4)	1	(0.1)
loratadine (+) pseudoephedrine sulfate	1	(0.2)	1	(0.4)	2	(0.3)
naphazoline hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
naphazoline nitrate (+) prednisolone	1	(0.2)	0	(0.0)	1	(0.1)
oxymetazoline hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
tetrahydrozoline hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
xylometazoline hydrochloride	2	(0.4)	2	(0.8)	4	(0.5)
throat preparations	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
benzoxonium chloride (+) lidocaine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
cetylpyridinium chloride (+) lidocaine hydrochloride (+) menthol	1	(0.2)	0	(0.0)	1	(0.1)
sensory organs						

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
sensory organs						
ophthalmologicals	**3**	**(0.6)**	**1**	**(0.4)**	**4**	**(0.5)**
acetazolamide	0	(0.0)	1	(0.4)	1	(0.1)
brimonidine tartrate (+) timolol maleate	1	(0.2)	0	(0.0)	1	(0.1)
ciprofloxacin (+) dexamethasone	1	(0.2)	0	(0.0)	1	(0.1)
dextran 70 (+) hypromellose	1	(0.2)	0	(0.0)	1	(0.1)
dorzolamide hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
systemic hormonal preparations, excl. sex hormones and insulins						
corticosteroids for systemic use	**9**	**(1.7)**	**7**	**(2.6)**	**16**	**(2.0)**
betamethasone	2	(0.4)	1	(0.4)	3	(0.4)
cortisone	0	(0.0)	1	(0.4)	1	(0.1)
cyanocobalamin (+) dexamethasone (+) lidocaine hydrochloride (+) thiamine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
dexamethasone	1	(0.2)	1	(0.4)	2	(0.3)
prednisolone	1	(0.2)	2	(0.8)	3	(0.4)
prednisone	3	(0.6)	1	(0.4)	4	(0.5)
triamcinolone	0	(0.0)	1	(0.4)	1	(0.1)
triamcinolone acetonide	2	(0.4)	0	(0.0)	2	(0.3)
thyroid therapy	**3**	**(0.6)**	**3**	**(1.1)**	**6**	**(0.8)**
levothyroxine sodium	3	(0.6)	3	(1.1)	6	(0.8)
various						
all other non-therapeutic products	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
allantoin (+) calendula (+) disodium laureth sulfosuccinate (+) sodium cocoyl isethionate (+) sodium laureth sulfate	0	(0.0)	1	(0.4)	1	(0.1)
all other therapeutic products	**19**	**(3.6)**	**14**	**(5.3)**	**33**	**(4.1)**
Antennaria dioica (+) Echinacea purpurea (+) field poppy (+) forskohlii (+) high mallow (+) marshmallow (+) mullein (+) Viola calcarata	0	(0.0)	1	(0.4)	1	(0.1)
Aphanizomenon flosaquae (+) bilberry (+) blueberry (+) caffeine (+) chlorella (+) chocolate (+) cranberry (+) damiana (+) Fragaria virginiana (+) grape (+) grape seeds (+) guarana (+) mate (+) plum (+) raspberry (+) rice (+) sour cherry	0	(0.0)	1	(0.4)	1	(0.1)
CT-102 activated platelet supernatant	1	(0.2)	0	(0.0)	1	(0.1)
Chinese skullcap (+) coptis (+) dandelion (+) gardenia (+) isatis (+) Japanese honeysuckle (+) knotweed (+) shrubby sophora (+) sweet wormwood (+) Tokyo violet (+) wild chrysanthemum	1	(0.2)	0	(0.0)	1	(0.1)
Plantago arenaria	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**19**	**(3.6)**	**14**	**(5.3)**	**33**	**(4.1)**
[composition unspecified]	3	(0.6)	0	(0.0)	3	(0.4)
acetylcysteine (+) arginine hydrochloride (+) glutamine (+) lysine hydrochloride (+) pidolic acid (+) schizonepeta	0	(0.0)	1	(0.4)	1	(0.1)
ajowan (+) anise (+) ascorbic acid (+) cinnamon (+) eucalyptus (+) fenugreek (+) garden daisy (+) grape (+) lemon (+) lesser galangal (+) mullein (+) oat (+) plantain (+) sage (+) thyme (+) turmeric	1	(0.2)	0	(0.0)	1	(0.1)
alfalfa (+) algae (+) amla (+) chocolate (+) coffee (+) eleuthero (+) fiber (+) fruit (+) ginkgo (+) grains (+) licorice (+) milk thistle (+) nigella (+) purslane (+) resveratrol (+) sea buckthorn (+) sunflower (+) tea (+) vegetables (+) xanthophyll	0	(0.0)	1	(0.4)	1	(0.1)
andrographis (+) dandelion (+) Japanese honeysuckle	1	(0.2)	0	(0.0)	1	(0.1)
anthocyanins (unspecified) (+) beta alanine (+) citrulline (+) creatine (+) rhodiola (+) schisandra (+) yohimbe	1	(0.2)	0	(0.0)	1	(0.1)
artichoke (+) calcium phosphate, dibasic (+) milk thistle (+) riboflavin (+) turmeric	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) Bacillus coagulans (+) butchers broom	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) dimethyl sulfone (+) ginger (+) glucosamine sulfate (+) manganese sulfate (+) white willow	1	(0.2)	0	(0.0)	1	(0.1)
astragalus (+) bai zhu atractylodes (+) bupleurum (+) chebulic myrobalan (+) Chinese cimicifuga (+) Chinese licorice (+) codonopsis (+) dong quai (+) magnolia (+) plantago seed (+) schisandra (+) schizonepeta (+) Sichuan lovage (+) siler (+) xanthium	1	(0.2)	0	(0.0)	1	(0.1)
astragalus (+) cleavers (+) dandelion (+) European elder (+) milk thistle (+) propolis (+) wild indigo	0	(0.0)	1	(0.4)	1	(0.1)
biotin (+) black currant (+) borage oil (+) cysteine (+) sodium selenite (+) zinc sulfate	0	(0.0)	1	(0.4)	1	(0.1)
caffeine (+) capsicum (+) catechu (+) damiana (+) guarana (+) mate (+) velvet bean	0	(0.0)	1	(0.4)	1	(0.1)
cats claw	0	(0.0)	1	(0.4)	1	(0.1)
chamomile	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Prior Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**19**	**(3.6)**	**14**	**(5.3)**	**33**	**(4.1)**
cholecalciferol (+) lactoferrin (as drug) (+) zinc oxide	0	(0.0)	1	(0.4)	1	(0.1)
chondroitin sulfate sodium (+) dimethyl sulfone (+) glucosamine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
chondroitin sulfate sodium (+) glucosamine sulfate	1	(0.2)	0	(0.0)	1	(0.1)
cranberry	1	(0.2)	0	(0.0)	1	(0.1)
dimethyl sulfone	1	(0.2)	0	(0.0)	1	(0.1)
echinacea (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
fulvic acid (+) glutamine (+) selenium (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
garcinia	1	(0.2)	0	(0.0)	1	(0.1)
ginkgo	0	(0.0)	1	(0.4)	1	(0.1)
ginseng (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
herbs (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
leucovorin calcium	0	(0.0)	2	(0.8)	2	(0.3)
potassium permanganate	1	(0.2)	0	(0.0)	1	(0.1)
prasterone	1	(0.2)	1	(0.4)	2	(0.3)
saw palmetto	1	(0.2)	0	(0.0)	1	(0.1)
spirulina	1	(0.2)	1	(0.4)	2	(0.3)
syrup of figs	1	(0.2)	0	(0.0)	1	(0.1)
trichloroacetic acid	0	(0.0)	1	(0.4)	1	(0.1)
contrast media	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
iopromide	1	(0.2)	0	(0.0)	1	(0.1)
general nutrients	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**
carbohydrates (unspecified) (+) fat (unspecified) (+) minerals (unspecified) (+) protein (unspecified) (+) vitamins (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
minerals (unspecified) (+) protein (unspecified) (+) vitamins (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
protein (unspecified)	2	(0.4)	1	(0.4)	3	(0.4)

Every subject is counted a single time for each applicable specific prior medication. A subject with multiple prior medications within a medication category is counted a single time for that category.

A medication class or specific medication appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 10

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
With one or more concomitant medications	447	(84.2)	240	(90.2)	687	(86.2)
With no concomitant medication	84	(15.8)	26	(9.8)	110	(13.8)
alimentary tract and metabolism						
anabolic agents for systemic use	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
nandrolone	0	(0.0)	1	(0.4)	1	(0.1)
stanozolol	0	(0.0)	1	(0.4)	1	(0.1)
antidiarrheals, intestinal antiinflammatory/antiinfective agents	**28**	**(5.3)**	**15**	**(5.6)**	**43**	**(5.4)**
Bacillus coagulans	1	(0.2)	0	(0.0)	1	(0.1)
Bifidobacterium animalis (+) Lactobacillus acidophilus	0	(0.0)	1	(0.4)	1	(0.1)
Bifidobacterium longum (+) fructooligosaccharides (+) Lactobacillus rhamnosus	1	(0.2)	0	(0.0)	1	(0.1)
Lactobacillus acidophilus	2	(0.4)	0	(0.0)	2	(0.3)
Lactobacillus acidophilus (+) Lactobacillus rhamnosus	1	(0.2)	0	(0.0)	1	(0.1)
Lactobacillus rhamnosus (+) Saccharomyces boulardii	1	(0.2)	0	(0.0)	1	(0.1)
Saccharomyces boulardii	3	(0.6)	0	(0.0)	3	(0.4)
attapulgite, activated (+) aminopentamide sulfate (+) bismuth subcarbonate (+) kanamycin sulfate (+) pectin	1	(0.2)	0	(0.0)	1	(0.1)
bismuth subsalicylate	2	(0.4)	3	(1.1)	5	(0.6)
citric acid (+) dextrose (+) fructose (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride (+) sucrose	1	(0.2)	0	(0.0)	1	(0.1)
dextrose (+) potassium chloride (+) sodium chloride (+) sodium citrate	1	(0.2)	1	(0.4)	2	(0.3)
fidaxomicin	0	(0.0)	1	(0.4)	1	(0.1)
gelatin tannate	1	(0.2)	0	(0.0)	1	(0.1)
kaolin (+) pectin	1	(0.2)	0	(0.0)	1	(0.1)
loperamide	6	(1.1)	2	(0.8)	8	(1.0)
loperamide hydrochloride	6	(1.1)	6	(2.3)	12	(1.5)
loperamide hydrochloride (+) simethicone	1	(0.2)	0	(0.0)	1	(0.1)
mesalamine	1	(0.2)	3	(1.1)	4	(0.5)
probiotics (unspecified)	3	(0.6)	2	(0.8)	5	(0.6)
racecadotril	1	(0.2)	0	(0.0)	1	(0.1)
rifaximin	2	(0.4)	0	(0.0)	2	(0.3)
smectite	2	(0.4)	0	(0.0)	2	(0.3)
antiemetics and antinauseants	**13**	**(2.4)**	**3**	**(1.1)**	**16**	**(2.0)**

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
antiemetics and antinauseants	**13**	**(2.4)**	**3**	**(1.1)**	**16**	**(2.0)**
dronabinol	1	(0.2)	0	(0.0)	1	(0.1)
granisetron hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
metopimazine	1	(0.2)	0	(0.0)	1	(0.1)
ondansetron	4	(0.8)	1	(0.4)	5	(0.6)
ondansetron hydrochloride	8	(1.5)	1	(0.4)	9	(1.1)
scopolamine	1	(0.2)	0	(0.0)	1	(0.1)
antiobesity preparations, excl. diet products	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
phentermine resinate	1	(0.2)	0	(0.0)	1	(0.1)
bile and liver therapy	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
arginine	0	(0.0)	1	(0.4)	1	(0.1)
homatropine methylbromide (+) menthol (+) methenamine (+) ox bile extract (+) papaverine hydrochloride (+) phenolphthalein	0	(0.0)	1	(0.4)	1	(0.1)
ursodiol	1	(0.2)	0	(0.0)	1	(0.1)
digestives, incl. enzymes	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
lactase	0	(0.0)	1	(0.4)	1	(0.1)
pancreatin	1	(0.2)	0	(0.0)	1	(0.1)
pancrelipase	0	(0.0)	1	(0.4)	1	(0.1)
drugs for acid related disorders	**64**	**(12.1)**	**48**	**(18.0)**	**112**	**(14.1)**
aluminum hydroxide (+) calcium carbonate (+) magnesium carbonate (+) magnesium trisilicate (+) sodium bicarbonate	1	(0.2)	0	(0.0)	1	(0.1)
aluminum hydroxide (+) dicyclomine hydrochloride (+) magnesium oxide	0	(0.0)	1	(0.4)	1	(0.1)
aluminum hydroxide (+) magnesium hydroxide (+) simethicone	3	(0.6)	0	(0.0)	3	(0.4)
calcium carbonate	0	(0.0)	2	(0.8)	2	(0.3)
calcium carbonate (+) magnesium carbonate	1	(0.2)	1	(0.4)	2	(0.3)
calcium carbonate (+) sodium alginate (+) sodium bicarbonate	1	(0.2)	0	(0.0)	1	(0.1)
citric acid (+) sodium bicarbonate (+) sodium carbonate	0	(0.0)	1	(0.4)	1	(0.1)
dexlansoprazole	1	(0.2)	2	(0.8)	3	(0.4)
esomeprazole	5	(0.9)	3	(1.1)	8	(1.0)
esomeprazole magnesium	5	(0.9)	2	(0.8)	7	(0.9)
famotidine	0	(0.0)	3	(1.1)	3	(0.4)
lansoprazole	7	(1.3)	3	(1.1)	10	(1.3)
magnesium oxide	1	(0.2)	1	(0.4)	2	(0.3)
misoprostol	0	(0.0)	1	(0.4)	1	(0.1)
omeprazole	28	(5.3)	22	(8.3)	50	(6.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
drugs for acid related disorders	**64**	**(12.1)**	**48**	**(18.0)**	**112**	**(14.1)**
omeprazole (+) sodium bicarbonate	0	(0.0)	1	(0.4)	1	(0.1)
omeprazole magnesium	1	(0.2)	0	(0.0)	1	(0.1)
pantoprazole	4	(0.8)	6	(2.3)	10	(1.3)
pantoprazole sodium	8	(1.5)	3	(1.1)	11	(1.4)
rabeprazole sodium	1	(0.2)	0	(0.0)	1	(0.1)
ranitidine	5	(0.9)	3	(1.1)	8	(1.0)
ranitidine hydrochloride	3	(0.6)	3	(1.1)	6	(0.8)
sucralfate	1	(0.2)	1	(0.4)	2	(0.3)
drugs for constipation	**23**	**(4.3)**	**7**	**(2.6)**	**30**	**(3.8)**
bisacodyl	2	(0.4)	1	(0.4)	3	(0.4)
castile soap (+) water, tap	1	(0.2)	0	(0.0)	1	(0.1)
docusate sodium	4	(0.8)	2	(0.8)	6	(0.8)
docusate sodium (+) senna	1	(0.2)	1	(0.4)	2	(0.3)
flaxseed	2	(0.4)	0	(0.0)	2	(0.3)
glycerin	1	(0.2)	0	(0.0)	1	(0.1)
lactulose	4	(0.8)	0	(0.0)	4	(0.5)
mineral oil	1	(0.2)	0	(0.0)	1	(0.1)
polyethylene glycol 3350	7	(1.3)	0	(0.0)	7	(0.9)
polyethylene glycol 3350 (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride	5	(0.9)	1	(0.4)	6	(0.8)
polyethylene glycol 3350 (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride (+) sodium sulfate	4	(0.8)	0	(0.0)	4	(0.5)
polyethylene glycol 4000	1	(0.2)	0	(0.0)	1	(0.1)
psyllium husk	3	(0.6)	2	(0.8)	5	(0.6)
sennosides	3	(0.6)	1	(0.4)	4	(0.5)
sodium phosphate, dibasic (+) sodium phosphate, monobasic	3	(0.6)	0	(0.0)	3	(0.4)
sterculia	2	(0.4)	0	(0.0)	2	(0.3)
drugs for functional gastrointestinal disorders	**31**	**(5.8)**	**13**	**(4.9)**	**44**	**(5.5)**
acetaminophen (+) butylscopolamine bromide	1	(0.2)	1	(0.4)	2	(0.3)
alizapride hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
butylscopolamine bromide	10	(1.9)	4	(1.5)	14	(1.8)
butylscopolamine bromide (+) dipyrone	1	(0.2)	0	(0.0)	1	(0.1)
charcoal, activated (+) simethicone	1	(0.2)	0	(0.0)	1	(0.1)
cinitapride bitartrate (+) pancreatin (+) simethicone	0	(0.0)	1	(0.4)	1	(0.1)
dicyclomine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
domperidone	3	(0.6)	0	(0.0)	3	(0.4)
mebeverine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
drugs for functional gastrointestinal disorders	**31**	**(5.8)**	**13**	**(4.9)**	**44**	**(5.5)**
metoclopramide	6	(1.1)	2	(0.8)	8	(1.0)
metoclopramide hydrochloride	6	(1.1)	2	(0.8)	8	(1.0)
pargeverine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
peppermint oil	1	(0.2)	0	(0.0)	1	(0.1)
phloroglucinol	1	(0.2)	1	(0.4)	2	(0.3)
phloroglucinol (+) trimethylphloroglucinol	1	(0.2)	0	(0.0)	1	(0.1)
simethicone	2	(0.4)	2	(0.8)	4	(0.5)
simethicone (+) trimebutine maleate	0	(0.0)	1	(0.4)	1	(0.1)
trimebutine	1	(0.2)	0	(0.0)	1	(0.1)
trimebutine maleate	1	(0.2)	0	(0.0)	1	(0.1)
drugs used in diabetes	**10**	**(1.9)**	**5**	**(1.9)**	**15**	**(1.9)**
glimepiride	1	(0.2)	1	(0.4)	2	(0.3)
glipizide	2	(0.4)	0	(0.0)	2	(0.3)
glyburide	2	(0.4)	1	(0.4)	3	(0.4)
guar gum	1	(0.2)	0	(0.0)	1	(0.1)
insulin aspart (+) insulin aspart protamine	0	(0.0)	1	(0.4)	1	(0.1)
insulin detemir	0	(0.0)	1	(0.4)	1	(0.1)
insulin glargine	2	(0.4)	1	(0.4)	3	(0.4)
insulin lispro	1	(0.2)	0	(0.0)	1	(0.1)
liraglutide	2	(0.4)	0	(0.0)	2	(0.3)
metformin	5	(0.9)	2	(0.8)	7	(0.9)
metformin hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
metformin hydrochloride (+) sitagliptin phosphate	2	(0.4)	0	(0.0)	2	(0.3)
metformin hydrochloride (+) vildagliptin	0	(0.0)	1	(0.4)	1	(0.1)
sitagliptin	1	(0.2)	0	(0.0)	1	(0.1)
mineral supplements	**18**	**(3.4)**	**16**	**(6.0)**	**34**	**(4.3)**
ascorbic acid (+) calcium gluconate (+) magnesium carbonate	1	(0.2)	0	(0.0)	1	(0.1)
calcium (unspecified) (+) cholecalciferol	1	(0.2)	0	(0.0)	1	(0.1)
calcium (unspecified) (+) magnesium (unspecified) (+) vitamin D (unspecified) (+) zinc (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
calcium (unspecified) (+) vitamin D (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
calcium carbonate (+) magnesium chloride	1	(0.2)	0	(0.0)	1	(0.1)
calcium citrate	1	(0.2)	0	(0.0)	1	(0.1)
calcium citrate (+) chromic chloride (+) copper citrate (+) ferrous citrate (+) magnesium citrate (+) potassium citrate (+) sodium citrate (+) sodium molybdate (+) sodium selenite (+) zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
mineral supplements	**18**	**(3.4)**	**16**	**(6.0)**	**34**	**(4.3)**
magnesium (unspecified)	0	(0.0)	3	(1.1)	3	(0.4)
magnesium pidolate	0	(0.0)	1	(0.4)	1	(0.1)
potassium (unspecified)	1	(0.2)	1	(0.4)	2	(0.3)
potassium aspartate	0	(0.0)	1	(0.4)	1	(0.1)
potassium bicarbonate (+) potassium citrate	0	(0.0)	1	(0.4)	1	(0.1)
potassium chloride	2	(0.4)	1	(0.4)	3	(0.4)
potassium gluconate	0	(0.0)	1	(0.4)	1	(0.1)
selenium (unspecified)	2	(0.4)	2	(0.8)	4	(0.5)
selenium (unspecified) (+) zinc picolinate	1	(0.2)	0	(0.0)	1	(0.1)
zinc (unspecified)	3	(0.6)	3	(1.1)	6	(0.8)
zinc acetate (+) zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)
zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)
zinc sulfate	2	(0.4)	1	(0.4)	3	(0.4)
other alimentary tract and metabolism products	**9**	**(1.7)**	**1**	**(0.4)**	**10**	**(1.3)**
ademetionine sulfate tosylate (+) cyanocobalamin (+) leucovorin calcium	1	(0.2)	0	(0.0)	1	(0.1)
amino acids (unspecified) (+) caffeine (+) tea	1	(0.2)	0	(0.0)	1	(0.1)
gastrointestinal preparations (unspecified)	3	(0.6)	0	(0.0)	3	(0.4)
glutamine	1	(0.2)	0	(0.0)	1	(0.1)
levocarnitine	0	(0.0)	1	(0.4)	1	(0.1)
lysine	2	(0.4)	1	(0.4)	3	(0.4)
xanthophyll (+) zeaxanthin	1	(0.2)	0	(0.0)	1	(0.1)
stomatological preparations	**9**	**(1.7)**	**3**	**(1.1)**	**12**	**(1.5)**
aloe vera (+) maltodextrin (+) potassium sorbate	1	(0.2)	1	(0.4)	2	(0.3)
aluminum hydroxide (+) ibuprofen (+) lidocaine (+) magnesium hydroxide	0	(0.0)	1	(0.4)	1	(0.1)
chlorhexidine hydrochloride (+) lidocaine (+) triamcinolone acetonide	1	(0.2)	0	(0.0)	1	(0.1)
diphenhydramine hydrochloride (+) lidocaine hydrochloride (+) nystatin	1	(0.2)	0	(0.0)	1	(0.1)
eucalyptol (+) menthol (+) methyl salicylate (+) thymol	1	(0.2)	0	(0.0)	1	(0.1)
hexetidine	2	(0.4)	0	(0.0)	2	(0.3)
metronidazole (+) spiramycin	3	(0.6)	1	(0.4)	4	(0.5)
vitamins	**104**	**(19.6)**	**56**	**(21.1)**	**160**	**(20.1)**

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
vitamins	**104**	**(19.6)**	**56**	**(21.1)**	**160**	**(20.1)**
acetylcysteine (+) bilberry (+) bioflavonoids (+) broccoli (+) bromelains (+) choline (+) cinnamon (+) inositol (+) lycopene (+) minerals (+) olive (+) pomegranate (+) tea (+) thioctic acid (+) turmeric (+) ubidecarenone (+) vitamins (+) xanthophyll	1	(0.2)	0	(0.0)	1	(0.1)
adenosine triphosphate (+) arginine aspartate (+) glutathione (+) hydroxocobalamin (+) lysine hydrochloride (+) pyritinol hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid	19	(3.6)	14	(5.3)	33	(4.1)
ascorbic acid (+) beta carotene (+) ergocalciferol (+) folic acid (+) vitamin B complex (+) vitamin E	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) bioflavonoids (+) calcium (+) chromium (+) copper (+) folic acid (+) iodine (+) iron (+) lysine (+) manganese (+) magnesium (+) selenium (+) vitamin A (+) vitamin B complex (+) vitamin D (+) zinc	2	(0.4)	0	(0.0)	2	(0.3)
ascorbic acid (+) calcium (unspecified) (+) chromium (unspecified) (+) folic acid (+) magnesium (unspecified) (+) manganese (unspecified) (+) potassium (unspecified) (+) thioctic acid (+) vitamin B complex (+) zinc (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
ascorbic acid (+) ferrous sulfate (+) folic acid (+) rutin (+) vitamin A (+) vitamin B complex (+) vitamin E (+) zinc sulfate	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) folic acid (+) vitamin B complex	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) vitamin B (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
astaxanthin (+) broccoli (+) cranberry (+) minerals (unspecified) (+) thioctic acid (+) vitamins (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
biotin	1	(0.2)	1	(0.4)	2	(0.3)
cholecalciferol	24	(4.5)	13	(4.9)	37	(4.6)
cyanocobalamin (+) pyridoxine (+) thiamine	3	(0.6)	1	(0.4)	4	(0.5)
dexpanthenol	2	(0.4)	0	(0.0)	2	(0.3)
ergocalciferol	2	(0.4)	1	(0.4)	3	(0.4)
ginseng (unspecified) (+) minerals (unspecified) (+) vitamins (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
minerals (unspecified) (+) vitamins (unspecified)	5	(0.9)	2	(0.8)	7	(0.9)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
alimentary tract and metabolism						
vitamins	**104**	**(19.6)**	**56**	**(21.1)**	**160**	**(20.1)**
pyridoxine	9	(1.7)	4	(1.5)	13	(1.6)
pyridoxine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
thiamine	1	(0.2)	1	(0.4)	2	(0.3)
vitamin A	0	(0.0)	1	(0.4)	1	(0.1)
vitamin B (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
vitamin B complex	7	(1.3)	8	(3.0)	15	(1.9)
vitamin D (unspecified)	15	(2.8)	6	(2.3)	21	(2.6)
vitamin E	4	(0.8)	1	(0.4)	5	(0.6)
vitamins (unspecified)	37	(7.0)	19	(7.1)	56	(7.0)
antiinfectives for systemic use						
antibacterials for systemic use	**236**	**(44.4)**	**139**	**(52.3)**	**375**	**(47.1)**
amoxicillin	38	(7.2)	19	(7.1)	57	(7.2)
amoxicillin (+) clavulanate potassium	39	(7.3)	25	(9.4)	64	(8.0)
ampicillin	0	(0.0)	1	(0.4)	1	(0.1)
ampicillin sodium (+) sulbactam sodium	1	(0.2)	0	(0.0)	1	(0.1)
antimicrobial (unspecified)	3	(0.6)	4	(1.5)	7	(0.9)
azithromycin	59	(11.1)	33	(12.4)	92	(11.5)
cefaclor	1	(0.2)	0	(0.0)	1	(0.1)
cefadroxil	2	(0.4)	2	(0.8)	4	(0.5)
cefazolin	3	(0.6)	1	(0.4)	4	(0.5)
cefazolin sodium	1	(0.2)	3	(1.1)	4	(0.5)
cefepime	0	(0.0)	2	(0.8)	2	(0.3)
cefixime	3	(0.6)	4	(1.5)	7	(0.9)
cefprozil	1	(0.2)	1	(0.4)	2	(0.3)
ceftazidime	0	(0.0)	1	(0.4)	1	(0.1)
ceftriaxone	30	(5.6)	17	(6.4)	47	(5.9)
ceftriaxone sodium	7	(1.3)	2	(0.8)	9	(1.1)
cefuroxime	2	(0.4)	6	(2.3)	8	(1.0)
cefuroxime axetil	0	(0.0)	3	(1.1)	3	(0.4)
cephalexin	8	(1.5)	9	(3.4)	17	(2.1)
chloramphenicol	3	(0.6)	2	(0.8)	5	(0.6)
ciprofloxacin	25	(4.7)	15	(5.6)	40	(5.0)
ciprofloxacin hydrochloride	4	(0.8)	1	(0.4)	5	(0.6)
clarithromycin	7	(1.3)	4	(1.5)	11	(1.4)
clavulanate potassium	1	(0.2)	0	(0.0)	1	(0.1)
clavulanic acid	0	(0.0)	1	(0.4)	1	(0.1)
clindamycin	8	(1.5)	5	(1.9)	13	(1.6)
clindamycin hydrochloride	2	(0.4)	1	(0.4)	3	(0.4)
clindamycin phosphate	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiinfectives for systemic use						
antibacterials for systemic use	**236**	**(44.4)**	**139**	**(52.3)**	**375**	**(47.1)**
cloxacillin	1	(0.2)	0	(0.0)	1	(0.1)
dalbavancin	1	(0.2)	0	(0.0)	1	(0.1)
daptomycin	1	(0.2)	0	(0.0)	1	(0.1)
dicloxacillin	3	(0.6)	1	(0.4)	4	(0.5)
doxycycline	36	(6.8)	22	(8.3)	58	(7.3)
doxycycline hyclate	3	(0.6)	2	(0.8)	5	(0.6)
ertapenem sodium	1	(0.2)	0	(0.0)	1	(0.1)
erythromycin	2	(0.4)	2	(0.8)	4	(0.5)
floxacillin	5	(0.9)	2	(0.8)	7	(0.9)
floxacillin sodium	1	(0.2)	0	(0.0)	1	(0.1)
fosfomycin	0	(0.0)	1	(0.4)	1	(0.1)
fusidate sodium	2	(0.4)	1	(0.4)	3	(0.4)
fusidic acid	2	(0.4)	1	(0.4)	3	(0.4)
gentamicin	1	(0.2)	1	(0.4)	2	(0.3)
gentamicin sulfate	0	(0.0)	1	(0.4)	1	(0.1)
levofloxacin	16	(3.0)	5	(1.9)	21	(2.6)
lincomycin hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
methacycline	1	(0.2)	0	(0.0)	1	(0.1)
metronidazole	28	(5.3)	12	(4.5)	40	(5.0)
minocycline	2	(0.4)	0	(0.0)	2	(0.3)
minocycline hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
moxifloxacin	7	(1.3)	5	(1.9)	12	(1.5)
moxifloxacin hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
nitrofurantoin	0	(0.0)	1	(0.4)	1	(0.1)
ofloxacin	4	(0.8)	1	(0.4)	5	(0.6)
penicillin (unspecified)	8	(1.5)	3	(1.1)	11	(1.4)
penicillin G	1	(0.2)	0	(0.0)	1	(0.1)
penicillin G benzathine	21	(4.0)	13	(4.9)	34	(4.3)
penicillin G benzathine (+) tolycaine hydrochloride	3	(0.6)	2	(0.8)	5	(0.6)
penicillin V	0	(0.0)	1	(0.4)	1	(0.1)
piperacillin sodium (+) tazobactam sodium	2	(0.4)	2	(0.8)	4	(0.5)
roxithromycin	1	(0.2)	2	(0.8)	3	(0.4)
spectinomycin hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
sulfadiazine	1	(0.2)	2	(0.8)	3	(0.4)
sulfamethoxazole	1	(0.2)	0	(0.0)	1	(0.1)
sulfamethoxazole (+) trimethoprim	49	(9.2)	33	(12.4)	82	(10.3)
sultamicillin	1	(0.2)	0	(0.0)	1	(0.1)
tinidazole	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiinfectives for systemic use						
antibacterials for systemic use	**236**	**(44.4)**	**139**	**(52.3)**	**375**	**(47.1)**
tobramycin	0	(0.0)	1	(0.4)	1	(0.1)
trimethoprim	2	(0.4)	0	(0.0)	2	(0.3)
vancomycin	0	(0.0)	3	(1.1)	3	(0.4)
antimycobacterials	**18**	**(3.4)**	**11**	**(4.1)**	**29**	**(3.6)**
aminosalicylic acid	0	(0.0)	1	(0.4)	1	(0.1)
dapsone	4	(0.8)	1	(0.4)	5	(0.6)
ethambutol	3	(0.6)	1	(0.4)	4	(0.5)
ethambutol hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
isoniazid	13	(2.4)	8	(3.0)	21	(2.6)
pyrazinamide	2	(0.4)	1	(0.4)	3	(0.4)
rifampin	1	(0.2)	1	(0.4)	2	(0.3)
antimycotics for systemic use	**13**	**(2.4)**	**16**	**(6.0)**	**29**	**(3.6)**
amphotericin B	0	(0.0)	2	(0.8)	2	(0.3)
fluconazole	12	(2.3)	12	(4.5)	24	(3.0)
itraconazole	1	(0.2)	3	(1.1)	4	(0.5)
antivirals for systemic use	**49**	**(9.2)**	**36**	**(13.5)**	**85**	**(10.7)**
abacavir	0	(0.0)	1	(0.4)	1	(0.1)
acyclovir	22	(4.1)	17	(6.4)	39	(4.9)
cobicistat (+) darunavir	1	(0.2)	1	(0.4)	2	(0.3)
cobicistat (+) elvitegravir (+) emtricitabine (+) tenofovir disoproxil fumarate	2	(0.4)	0	(0.0)	2	(0.3)
dolutegravir	0	(0.0)	1	(0.4)	1	(0.1)
efavirenz (+) emtricitabine (+) tenofovir disoproxil fumarate	2	(0.4)	0	(0.0)	2	(0.3)
emtricitabine (+) tenofovir disoproxil fumarate	2	(0.4)	2	(0.8)	4	(0.5)
famciclovir	0	(0.0)	3	(1.1)	3	(0.4)
ganciclovir	1	(0.2)	0	(0.0)	1	(0.1)
lamivudine	1	(0.2)	1	(0.4)	2	(0.3)
lopinavir (+) ritonavir	1	(0.2)	0	(0.0)	1	(0.1)
nevirapine	1	(0.2)	0	(0.0)	1	(0.1)
oseltamivir	1	(0.2)	1	(0.4)	2	(0.3)
oseltamivir phosphate	1	(0.2)	3	(1.1)	4	(0.5)
raltegravir potassium	1	(0.2)	1	(0.4)	2	(0.3)
tenofovir	1	(0.2)	0	(0.0)	1	(0.1)
valacyclovir hydrochloride	15	(2.8)	13	(4.9)	28	(3.5)
vaccines	**139**	**(26.2)**	**62**	**(23.3)**	**201**	**(25.2)**
HPV rL1 6 11 16 18 VLP vaccine (yeast)	3	(0.6)	2	(0.8)	5	(0.6)
HPV vaccine (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
diphtheria toxoid (+) pertussis acellular 3-component vaccine (+) tetanus toxoid	4	(0.8)	3	(1.1)	7	(0.9)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiinfectives for systemic use						
vaccines	**139**	**(26.2)**	**62**	**(23.3)**	**201**	**(25.2)**
diphtheria toxoid (+) pertussis acellular 5-component vaccine (+) poliovirus vaccine inactivated (Vero) (+) tetanus toxoid	0	(0.0)	3	(1.1)	3	(0.4)
diphtheria toxoid (+) pertussis acellular 5-component vaccine (+) tetanus toxoid	1	(0.2)	0	(0.0)	1	(0.1)
diphtheria toxoid (+) pertussis acellular vaccine (unspecified) (+) tetanus toxoid	3	(0.6)	1	(0.4)	4	(0.5)
diphtheria toxoid (+) pertussis vaccine (unspecified) (+) tetanus toxoid	3	(0.6)	0	(0.0)	3	(0.4)
diphtheria toxoid (+) poliovirus vaccine inactivated (Vero) (+) tetanus toxoid	1	(0.2)	2	(0.8)	3	(0.4)
diphtheria toxoid (+) poliovirus vaccine inactivated (unspecified) (+) tetanus toxoid	0	(0.0)	1	(0.4)	1	(0.1)
diphtheria toxoid (+) tetanus toxoid	2	(0.4)	0	(0.0)	2	(0.3)
hepatitis A virus vaccine (unspecified)	2	(0.4)	6	(2.3)	8	(1.0)
hepatitis A virus vaccine (unspecified) (+) hepatitis B virus vaccine (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
hepatitis A virus vaccine inactivated	4	(0.8)	1	(0.4)	5	(0.6)
hepatitis A virus vaccine inactivated (+) hepatitis B virus vaccine rHBsAg (yeast)	8	(1.5)	4	(1.5)	12	(1.5)
hepatitis B virus vaccine (unspecified)	11	(2.1)	8	(3.0)	19	(2.4)
hepatitis B virus vaccine plasma-derived	1	(0.2)	2	(0.8)	3	(0.4)
hepatitis B virus vaccine rHBsAg (yeast)	6	(1.1)	3	(1.1)	9	(1.1)
influenza virus sAg 3v vaccine inactivated	22	(4.1)	11	(4.1)	33	(4.1)
influenza virus split virion 3v vaccine inactivated	32	(6.0)	15	(5.6)	47	(5.9)
influenza virus split virion 4v vaccine inactivated	3	(0.6)	0	(0.0)	3	(0.4)
influenza virus vaccine (unspecified)	60	(11.3)	23	(8.6)	83	(10.4)
influenza virus vaccine inactivated (unspecified)	2	(0.4)	1	(0.4)	3	(0.4)
measles virus vaccine live (Enders-Edmonston) (+) mumps virus vaccine live (Jeryl Lynn) (+) rubella virus vaccine live (Wistar RA 27/3)	1	(0.2)	0	(0.0)	1	(0.1)
measles virus vaccine live (Schwartz) (+) mumps virus vaccine live (RIT 4385) (+) rubella virus vaccine live (Wistar RA 27/3)	3	(0.6)	0	(0.0)	3	(0.4)
measles virus vaccine live (unspecified) (+) mumps virus vaccine live (unspecified) (+) rubella virus vaccine live (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
meningococcal ACYW conj vaccine (CRM197)	2	(0.4)	0	(0.0)	2	(0.3)
meningococcal ACYW conj vaccine (dip toxoid)	1	(0.2)	0	(0.0)	1	(0.1)
meningococcal ACYW conj vaccine (tet toxoid)	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiinfectives for systemic use						
vaccines	**139**	**(26.2)**	**62**	**(23.3)**	**201**	**(25.2)**
meningococcal vaccine (unspecified)	1	(0.2)	1	(0.4)	2	(0.3)
pneumococcal 13v conj vaccine (CRM197)	11	(2.1)	7	(2.6)	18	(2.3)
pneumococcal 23v polysaccharide vaccine	11	(2.1)	7	(2.6)	18	(2.3)
pneumococcal 4 6B 9V 14 18C 19F 23F conj vaccine (CRM197)	15	(2.8)	6	(2.3)	21	(2.6)
pneumococcal vaccine (unspecified)	8	(1.5)	3	(1.1)	11	(1.4)
poliovirus vaccine inactivated (Vero)	1	(0.2)	0	(0.0)	1	(0.1)
rabies virus vaccine (Vero)	1	(0.2)	0	(0.0)	1	(0.1)
tetanus toxoid	4	(0.8)	1	(0.4)	5	(0.6)
tick-borne encephalitis virus vaccine	1	(0.2)	0	(0.0)	1	(0.1)
typhoid Vi polysaccharide vaccine	1	(0.2)	1	(0.4)	2	(0.3)
varicella virus vaccine live (Oka/RIT)	0	(0.0)	1	(0.4)	1	(0.1)
antineoplastic and immunomodulating agents						
antineoplastic agents	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
fluorouracil	1	(0.2)	0	(0.0)	1	(0.1)
hydroxyurea	1	(0.2)	0	(0.0)	1	(0.1)
endocrine therapy	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
tamoxifen	0	(0.0)	1	(0.4)	1	(0.1)
immunostimulants	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
filgrastim	0	(0.0)	1	(0.4)	1	(0.1)
immunosuppressants	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
tacrolimus	0	(0.0)	1	(0.4)	1	(0.1)
antiparasitic products, insecticides, and repellents						
anthelmintics	**2**	**(0.4)**	**3**	**(1.1)**	**5**	**(0.6)**
albendazole	1	(0.2)	1	(0.4)	2	(0.3)
ivermectin	1	(0.2)	2	(0.8)	3	(0.4)
antiprotozoals	**8**	**(1.5)**	**8**	**(3.0)**	**16**	**(2.0)**
atovaquone	3	(0.6)	3	(1.1)	6	(0.8)
atovaquone (+) chlorguanide hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
nitazoxanide	2	(0.4)	0	(0.0)	2	(0.3)
pentamidine isethionate	0	(0.0)	2	(0.8)	2	(0.3)
pyrimethamine	2	(0.4)	3	(1.1)	5	(0.6)
tilbroquinol (+) tiliquinol (+) tiliquinol lauryl sulfate	1	(0.2)	0	(0.0)	1	(0.1)
ectoparasticides, incl. scabicides, insecticides and repellents	**2**	**(0.4)**	**4**	**(1.5)**	**6**	**(0.8)**
benzyl benzoate	1	(0.2)	1	(0.4)	2	(0.3)
permethrin	1	(0.2)	2	(0.8)	3	(0.4)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
antiparasitic products, insecticides, and repellents						
ectoparasticides, incl. scabicides, insecticides and repellents	**2**	**(0.4)**	**4**	**(1.5)**	**6**	**(0.8)**
permethrin (+) piperonyl butoxide	0	(0.0)	1	(0.4)	1	(0.1)
blood and blood forming organs						
antianemic preparations	**18**	**(3.4)**	**9**	**(3.4)**	**27**	**(3.4)**
5-methyltetrahydrofolate (+) biotin (+) carbonyl iron (+) cyanocobalamin (+) docusate sodium (+) ferrous bisglycinate (+) magnesium ascorbate (+) zinc glycinate	2	(0.4)	0	(0.0)	2	(0.3)
ascorbic acid (+) beta carotene (+) calcium carbonate (+) carbonyl iron (+) cholecalciferol (+) copper (unspecified) (+) docusate sodium (+) folic acid (+) magnesium oxide (+) vitamin B complex (+) vitamin E acetate (+) zinc oxide	0	(0.0)	1	(0.4)	1	(0.1)
cyanocobalamin	4	(0.8)	3	(1.1)	7	(0.9)
ferric carboxymaltose	1	(0.2)	0	(0.0)	1	(0.1)
ferrous fumarate	0	(0.0)	2	(0.8)	2	(0.3)
ferrous sulfate	3	(0.6)	1	(0.4)	4	(0.5)
folic acid	8	(1.5)	2	(0.8)	10	(1.3)
iron (unspecified)	6	(1.1)	1	(0.4)	7	(0.9)
mecobalamin	2	(0.4)	0	(0.0)	2	(0.3)
antihemorrhagics	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
tranexamic acid	1	(0.2)	1	(0.4)	2	(0.3)
antithrombotic agents	**10**	**(1.9)**	**5**	**(1.9)**	**15**	**(1.9)**
alteplase (+) dornase alfa	1	(0.2)	0	(0.0)	1	(0.1)
certoparin sodium	1	(0.2)	1	(0.4)	2	(0.3)
clopidogrel	1	(0.2)	1	(0.4)	2	(0.3)
enoxaparin sodium	2	(0.4)	3	(1.1)	5	(0.6)
heparin	2	(0.4)	0	(0.0)	2	(0.3)
nadroparin calcium	0	(0.0)	1	(0.4)	1	(0.1)
rivaroxaban	3	(0.6)	0	(0.0)	3	(0.4)
ticagrelor	1	(0.2)	0	(0.0)	1	(0.1)
warfarin sodium	1	(0.2)	0	(0.0)	1	(0.1)
blood substitutes and perfusion solutions	**18**	**(3.4)**	**5**	**(1.9)**	**23**	**(2.9)**
dextrose (+) electrolytes (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
dextrose (+) sodium chloride	1	(0.2)	0	(0.0)	1	(0.1)
electrolytes (unspecified) (+) sodium lactate	3	(0.6)	0	(0.0)	3	(0.4)
platelet concentrate	0	(0.0)	1	(0.4)	1	(0.1)
sodium chloride	16	(3.0)	3	(1.1)	19	(2.4)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
cardiovascular system						
agents acting on the renin-angiotensin system	**37**	**(7.0)**	**19**	**(7.1)**	**56**	**(7.0)**
amlodipine besylate (+) benazepril hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
amlodipine besylate (+) valsartan	1	(0.2)	2	(0.8)	3	(0.4)
benazepril hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
candesartan	0	(0.0)	1	(0.4)	1	(0.1)
candesartan cilexetil	1	(0.2)	0	(0.0)	1	(0.1)
candesartan cilexetil (+) hydrochlorothiazide	1	(0.2)	0	(0.0)	1	(0.1)
captopril	0	(0.0)	1	(0.4)	1	(0.1)
enalapril	8	(1.5)	3	(1.1)	11	(1.4)
hydrochlorothiazide (+) lisinopril	1	(0.2)	0	(0.0)	1	(0.1)
hydrochlorothiazide (+) losartan potassium	0	(0.0)	1	(0.4)	1	(0.1)
hydrochlorothiazide (+) olmesartan medoxomil	0	(0.0)	1	(0.4)	1	(0.1)
indapamide (+) perindopril erbumine	2	(0.4)	1	(0.4)	3	(0.4)
lisinopril	12	(2.3)	4	(1.5)	16	(2.0)
losartan	4	(0.8)	3	(1.1)	7	(0.9)
losartan potassium	1	(0.2)	0	(0.0)	1	(0.1)
olmesartan medoxomil	1	(0.2)	0	(0.0)	1	(0.1)
perindopril	1	(0.2)	0	(0.0)	1	(0.1)
perindopril erbumine	2	(0.4)	1	(0.4)	3	(0.4)
ramipril	3	(0.6)	3	(1.1)	6	(0.8)
trandolapril	1	(0.2)	0	(0.0)	1	(0.1)
valsartan	0	(0.0)	1	(0.4)	1	(0.1)
antihypertensives	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
clonidine	0	(0.0)	1	(0.4)	1	(0.1)
hydralazine	1	(0.2)	0	(0.0)	1	(0.1)
beta blocking agents	**19**	**(3.6)**	**8**	**(3.0)**	**27**	**(3.4)**
atenolol	3	(0.6)	1	(0.4)	4	(0.5)
bisoprolol	5	(0.9)	4	(1.5)	9	(1.1)
bisoprolol fumarate	3	(0.6)	0	(0.0)	3	(0.4)
carvedilol	4	(0.8)	1	(0.4)	5	(0.6)
metoprolol	3	(0.6)	1	(0.4)	4	(0.5)
metoprolol tartrate	2	(0.4)	0	(0.0)	2	(0.3)
nebivolol	0	(0.0)	1	(0.4)	1	(0.1)
propranolol hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
calcium channel blockers	**14**	**(2.6)**	**9**	**(3.4)**	**23**	**(2.9)**
amlodipine	7	(1.3)	4	(1.5)	11	(1.4)
amlodipine besylate	3	(0.6)	3	(1.1)	6	(0.8)
diltiazem	2	(0.4)	0	(0.0)	2	(0.3)
felodipine	0	(0.0)	2	(0.8)	2	(0.3)
nifedipine	2	(0.4)	0	(0.0)	2	(0.3)
nitrendipine	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
cardiovascular system						
cardiac therapy	**4**	**(0.8)**	**1**	**(0.4)**	**5**	**(0.6)**
dofetilide	1	(0.2)	0	(0.0)	1	(0.1)
nitroglycerin	1	(0.2)	0	(0.0)	1	(0.1)
ubidecarenone	1	(0.2)	1	(0.4)	2	(0.3)
ubiquinol	1	(0.2)	0	(0.0)	1	(0.1)
diuretics	**10**	**(1.9)**	**4**	**(1.5)**	**14**	**(1.8)**
furosemide	1	(0.2)	0	(0.0)	1	(0.1)
hydrochlorothiazide	9	(1.7)	3	(1.1)	12	(1.5)
indapamide	1	(0.2)	1	(0.4)	2	(0.3)
piretanide	0	(0.0)	1	(0.4)	1	(0.1)
lipid modifying agents	**38**	**(7.2)**	**17**	**(6.4)**	**55**	**(6.9)**
amlodipine besylate (+) atorvastatin calcium	0	(0.0)	1	(0.4)	1	(0.1)
atorvastatin	3	(0.6)	1	(0.4)	4	(0.5)
atorvastatin calcium	5	(0.9)	1	(0.4)	6	(0.8)
black currant seed oil (+) borage oil (+) evening primrose oil (+) flaxseed (+) omega-3 marine triglycerides	1	(0.2)	1	(0.4)	2	(0.3)
borage oil (+) flaxseed (+) omega-3 marine triglycerides (+) vitamin E	1	(0.2)	0	(0.0)	1	(0.1)
ciprofibrate	0	(0.0)	2	(0.8)	2	(0.3)
fenofibrate	3	(0.6)	1	(0.4)	4	(0.5)
fenofibric acid	1	(0.2)	0	(0.0)	1	(0.1)
icosapent ethyl	1	(0.2)	0	(0.0)	1	(0.1)
lovastatin	1	(0.2)	0	(0.0)	1	(0.1)
niacin	1	(0.2)	0	(0.0)	1	(0.1)
omega-3 acid ethyl esters	1	(0.2)	1	(0.4)	2	(0.3)
omega-3 marine triglycerides	17	(3.2)	5	(1.9)	22	(2.8)
pravastatin	1	(0.2)	1	(0.4)	2	(0.3)
rosuvastatin	3	(0.6)	0	(0.0)	3	(0.4)
rosuvastatin calcium	3	(0.6)	4	(1.5)	7	(0.9)
simvastatin	3	(0.6)	2	(0.8)	5	(0.6)
peripheral vasodilators	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
pentoxifylline	0	(0.0)	1	(0.4)	1	(0.1)
vasoprotectives	**9**	**(1.7)**	**4**	**(1.5)**	**13**	**(1.6)**
calcium magnesium potassium carbonate chloride hydroxide (+) diosmin	1	(0.2)	0	(0.0)	1	(0.1)
carrageenan (+) titanium dioxide (+) zinc oxide	1	(0.2)	0	(0.0)	1	(0.1)
cocoa butter (+) phenylephrine hydrochloride (+) shark liver oil	0	(0.0)	1	(0.4)	1	(0.1)
dibucaine hydrochloride (+) esculin (+) framycetin sulfate (+) hydrocortisone	1	(0.2)	1	(0.4)	2	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
cardiovascular system						
vasoprotectives	**9**	**(1.7)**	**4**	**(1.5)**	**13**	**(1.6)**
dibucaine hydrochloride (+) policresulen	1	(0.2)	0	(0.0)	1	(0.1)
dibucaine hydrochloride (+) prednisolone hexanoate	1	(0.2)	0	(0.0)	1	(0.1)
diosmin (+) hesperidin	3	(0.6)	1	(0.4)	4	(0.5)
fluocortolone pivalate (+) lidocaine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
ruscogenin (+) trimebutine maleate	2	(0.4)	0	(0.0)	2	(0.3)
dermatologicals						
anti-acne preparations	**6**	**(1.1)**	**1**	**(0.4)**	**7**	**(0.9)**
adapalene	1	(0.2)	0	(0.0)	1	(0.1)
azelaic acid	1	(0.2)	0	(0.0)	1	(0.1)
benzoyl peroxide	2	(0.4)	0	(0.0)	2	(0.3)
benzoyl peroxide (+) clindamycin phosphate	1	(0.2)	0	(0.0)	1	(0.1)
isotretinoin	1	(0.2)	1	(0.4)	2	(0.3)
tretinoin	1	(0.2)	0	(0.0)	1	(0.1)
antibiotics and chemotherapeutics for dermatological use	**20**	**(3.8)**	**6**	**(2.3)**	**26**	**(3.3)**
bacitracin	2	(0.4)	0	(0.0)	2	(0.3)
bacitracin zinc	1	(0.2)	0	(0.0)	1	(0.1)
bacitracin zinc (+) neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
bacitracin zinc (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
hyaluronate sodium (+) sulfadiazine, silver	1	(0.2)	0	(0.0)	1	(0.1)
imiquimod	9	(1.7)	1	(0.4)	10	(1.3)
mupirocin	3	(0.6)	3	(1.1)	6	(0.8)
neomycin sulfate (+) tyrothricin	1	(0.2)	0	(0.0)	1	(0.1)
podofilox	1	(0.2)	1	(0.4)	2	(0.3)
podophyllum resin	2	(0.4)	1	(0.4)	3	(0.4)
sinecatechins	1	(0.2)	0	(0.0)	1	(0.1)
antifungals for dermatological use	**51**	**(9.6)**	**22**	**(8.3)**	**73**	**(9.2)**
amorolfine	1	(0.2)	1	(0.4)	2	(0.3)
amorolfine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
betamethasone dipropionate (+) clotrimazole	2	(0.4)	2	(0.8)	4	(0.5)
betamethasone dipropionate (+) clotrimazole (+) gentamicin sulfate	1	(0.2)	1	(0.4)	2	(0.3)
bifonazole (+) urea	0	(0.0)	1	(0.4)	1	(0.1)
ciclopirox	2	(0.4)	1	(0.4)	3	(0.4)
ciclopirox olamine	0	(0.0)	3	(1.1)	3	(0.4)
clotrimazole	18	(3.4)	4	(1.5)	22	(2.8)
clotrimazole (+) hexamidine isethionate	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
dermatologicals						
antifungals for dermatological use	**51**	**(9.6)**	**22**	**(8.3)**	**73**	**(9.2)**
econazole	4	(0.8)	0	(0.0)	4	(0.5)
econazole nitrate (+) triamcinolone acetonide	0	(0.0)	1	(0.4)	1	(0.1)
efinaconazole	0	(0.0)	1	(0.4)	1	(0.1)
griseofulvin	1	(0.2)	0	(0.0)	1	(0.1)
ketoconazole	6	(1.1)	5	(1.9)	11	(1.4)
lactic acid (+) salicylic acid	0	(0.0)	1	(0.4)	1	(0.1)
naftifine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
nystatin	5	(0.9)	2	(0.8)	7	(0.9)
terbinafine	11	(2.1)	1	(0.4)	12	(1.5)
terbinafine hydrochloride	3	(0.6)	1	(0.4)	4	(0.5)
tolnaftate	1	(0.2)	0	(0.0)	1	(0.1)
antipruritics, incl. antihistamines, anesthetics, etc.	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
benzalkonium chloride (+) lidocaine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
calamine (+) zinc oxide	1	(0.2)	0	(0.0)	1	(0.1)
antipsoriatics	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.4)**
acitretin	1	(0.2)	0	(0.0)	1	(0.1)
coal tar	1	(0.2)	0	(0.0)	1	(0.1)
tacalcitol	1	(0.2)	0	(0.0)	1	(0.1)
antiseptics and disinfectants	**12**	**(2.3)**	**2**	**(0.8)**	**14**	**(1.8)**
benzalkonium chloride (+) chlorhexidine hydrochloride (+) isopropyl myristate (+) mineral oil	1	(0.2)	0	(0.0)	1	(0.1)
cetostearyl alcohol (+) phenoxyethanol (+) sodium lauryl sulfate	1	(0.2)	0	(0.0)	1	(0.1)
chlorhexidine gluconate	3	(0.6)	0	(0.0)	3	(0.4)
glycerin (+) phenol	1	(0.2)	0	(0.0)	1	(0.1)
octenidine hydrochloride (+) phenoxyethanol	0	(0.0)	1	(0.4)	1	(0.1)
povidone-iodine	3	(0.6)	0	(0.0)	3	(0.4)
thymol	1	(0.2)	1	(0.4)	2	(0.3)
triclocarban	1	(0.2)	0	(0.0)	1	(0.1)
zinc oxide	1	(0.2)	0	(0.0)	1	(0.1)
corticosteroids, dermatological preparations	**43**	**(8.1)**	**24**	**(9.0)**	**67**	**(8.4)**
bacitracin zinc (+) hydrocortisone (+) neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
beclomethasone dipropionate (+) neomycin sulfate	1	(0.2)	0	(0.0)	1	(0.1)
betamethasone dipropionate	2	(0.4)	2	(0.8)	4	(0.5)
betamethasone dipropionate (+) calcipotriene	2	(0.4)	0	(0.0)	2	(0.3)
betamethasone dipropionate (+) fusidic acid	0	(0.0)	1	(0.4)	1	(0.1)
betamethasone dipropionate (+) gentamicin sulfate	1	(0.2)	1	(0.4)	2	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
dermatologicals						
corticosteroids, dermatological preparations	**43**	**(8.1)**	**24**	**(9.0)**	**67**	**(8.4)**
betamethasone valerate	6	(1.1)	3	(1.1)	9	(1.1)
betamethasone valerate (+) fusidic acid	3	(0.6)	4	(1.5)	7	(0.9)
camphor (+) clobetasol propionate (+) menthol	1	(0.2)	0	(0.0)	1	(0.1)
camphor (+) menthol (+) mometasone furoate	1	(0.2)	0	(0.0)	1	(0.1)
chlorhexidine hydrochloride (+) dexamethasone (+) nystatin	1	(0.2)	0	(0.0)	1	(0.1)
clobetasol propionate	6	(1.1)	3	(1.1)	9	(1.1)
clobetasone butyrate	0	(0.0)	1	(0.4)	1	(0.1)
coal tar (+) triamcinolone acetonide	1	(0.2)	0	(0.0)	1	(0.1)
desonide	1	(0.2)	0	(0.0)	1	(0.1)
desoximetasone	1	(0.2)	0	(0.0)	1	(0.1)
diflucortolone valerate	1	(0.2)	0	(0.0)	1	(0.1)
difluprednate	1	(0.2)	0	(0.0)	1	(0.1)
flumethasone pivalate (+) triclosan	1	(0.2)	0	(0.0)	1	(0.1)
fluorometholone	2	(0.4)	0	(0.0)	2	(0.3)
fluprednidene acetate (+) miconazole nitrate	0	(0.0)	1	(0.4)	1	(0.1)
gramicidin (+) neomycin sulfate (+) nystatin (+) triamcinolone acetonide	0	(0.0)	1	(0.4)	1	(0.1)
halometasone monohydrate	1	(0.2)	0	(0.0)	1	(0.1)
hydrocortisone acetate	12	(2.3)	3	(1.1)	15	(1.9)
hydrocortisone acetate (+) neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
hydrocortisone acetate (+) pramoxine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
hydrocortisone butyrate	1	(0.2)	0	(0.0)	1	(0.1)
hydrocortisone valerate	0	(0.0)	1	(0.4)	1	(0.1)
methylprednisolone aceponate	1	(0.2)	0	(0.0)	1	(0.1)
mometasone furoate	4	(0.8)	5	(1.9)	9	(1.1)
prednicarbate	0	(0.0)	1	(0.4)	1	(0.1)
emollients and protectives	**15**	**(2.8)**	**2**	**(0.8)**	**17**	**(2.1)**
almond oil (+) cetyl alcohol (+) dimethicone (+) glycerin (+) petrolatum (+) propylene glycol (+) vitamin E	1	(0.2)	0	(0.0)	1	(0.1)
aloe vera	2	(0.4)	0	(0.0)	2	(0.3)
bismuth subgallate (+) zinc oxide	1	(0.2)	0	(0.0)	1	(0.1)
caprylyl glycol (+) dimethicone (+) fireweed (+) glycerin (+) hyaluronate sodium (+) mineral oil (+) shea butter (+) zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)
cetyl alcohol (+) glyceryl monostearate (+) mineral oil (+) stearyl alcohol	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
dermatologicals						
emollients and protectives	**15**	**(2.8)**	**2**	**(0.8)**	**17**	**(2.1)**
coconut oil	1	(0.2)	0	(0.0)	1	(0.1)
copper gluconate (+) dimethicone (+) glycerin (+) hyaluronate sodium (+) madecassoside (+) manganese gluconate (+) panthenol (+) zinc gluconate	1	(0.2)	0	(0.0)	1	(0.1)
cupric sulfate (+) oat (+) zinc oxide (+) zinc sulfate	1	(0.2)	0	(0.0)	1	(0.1)
decyl oleate (+) isopropyl myristate (+) mineral oil (+) soysterol (+) vitamin E acetate	1	(0.2)	0	(0.0)	1	(0.1)
dimethicone (+) lactic acid (+) medium-chain triglycerides (+) mineral oil (+) myristyl lactate (+) sodium lactate	1	(0.2)	0	(0.0)	1	(0.1)
glycerin (+) mineral oil (+) petrolatum, white	1	(0.2)	1	(0.4)	2	(0.3)
mineral oil (+) petrolatum	1	(0.2)	0	(0.0)	1	(0.1)
mineral oil (+) petrolatum, white (+) wax, emulsifying	0	(0.0)	1	(0.4)	1	(0.1)
petrolatum, white	1	(0.2)	0	(0.0)	1	(0.1)
petrolatum, white (+) salicylic acid	1	(0.2)	0	(0.0)	1	(0.1)
polidocanol (+) urea	1	(0.2)	0	(0.0)	1	(0.1)
urea	2	(0.4)	0	(0.0)	2	(0.3)
other dermatological preparations	**6**	**(1.1)**	**5**	**(1.9)**	**11**	**(1.4)**
ammonium lactate	1	(0.2)	1	(0.4)	2	(0.3)
chloroacetic acid	1	(0.2)	0	(0.0)	1	(0.1)
chlorophyll	1	(0.2)	0	(0.0)	1	(0.1)
dermatologic (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
docusate sodium (+) lauromacrogol 400 (+) monoethanolamine (+) undecylenic acid (+) zinc undecylenate	1	(0.2)	0	(0.0)	1	(0.1)
minoxidil	0	(0.0)	2	(0.8)	2	(0.3)
pimecrolimus	0	(0.0)	1	(0.4)	1	(0.1)
sodium phenolsulfonic acid phenol formaldehyde urea condensate	1	(0.2)	1	(0.4)	2	(0.3)
preparations for the treatment of wounds and ulcers	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
bromelains	0	(0.0)	1	(0.4)	1	(0.1)
genitourinary system and sex hormones						
gynecological antiinfectives and antiseptics	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
furazolidone	1	(0.2)	0	(0.0)	1	(0.1)
other gynecologicals	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
genitourinary system and sex hormones						
other gynecologicals	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
relaxin	1	(0.2)	0	(0.0)	1	(0.1)
sex hormones and modulators of the genital system	**39**	**(7.3)**	**16**	**(6.0)**	**55**	**(6.9)**
chlormadinone acetate (+) ethinyl estradiol	0	(0.0)	1	(0.4)	1	(0.1)
cyproterone acetate (+) ethinyl estradiol	1	(0.2)	1	(0.4)	2	(0.3)
drospirenone (+) ethinyl estradiol	1	(0.2)	0	(0.0)	1	(0.1)
ethinyl estradiol (+) ferrous fumarate (+) norethindrone acetate	1	(0.2)	0	(0.0)	1	(0.1)
ethinyl estradiol (+) gestodene	2	(0.4)	0	(0.0)	2	(0.3)
ethinyl estradiol (+) levonorgestrel	1	(0.2)	1	(0.4)	2	(0.3)
ethinyl estradiol (+) norgestimate	1	(0.2)	0	(0.0)	1	(0.1)
etonogestrel implant	1	(0.2)	1	(0.4)	2	(0.3)
gonadotropin, chorionic	0	(0.0)	1	(0.4)	1	(0.1)
levonorgestrel	1	(0.2)	0	(0.0)	1	(0.1)
medroxyprogesterone acetate	22	(4.1)	5	(1.9)	27	(3.4)
norethindrone enanthate	6	(1.1)	0	(0.0)	6	(0.8)
testosterone	2	(0.4)	7	(2.6)	9	(1.1)
testosterone cypionate	3	(0.6)	0	(0.0)	3	(0.4)
testosterone enanthate	1	(0.2)	1	(0.4)	2	(0.3)
urologicals	**16**	**(3.0)**	**21**	**(7.9)**	**37**	**(4.6)**
alfuzosin hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
citric acid (+) sodium bicarbonate (+) sodium citrate (+) tartaric acid	1	(0.2)	0	(0.0)	1	(0.1)
finasteride	3	(0.6)	5	(1.9)	8	(1.0)
flavoxate hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
phenazopyridine hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
sildenafil citrate	4	(0.8)	5	(1.9)	9	(1.1)
solifenacin succinate	0	(0.0)	1	(0.4)	1	(0.1)
tadalafil	2	(0.4)	4	(1.5)	6	(0.8)
tamsulosin hydrochloride	4	(0.8)	2	(0.8)	6	(0.8)
vardenafil	0	(0.0)	1	(0.4)	1	(0.1)
vardenafil hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
musculoskeletal system						
antigout preparations	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
allopurinol	2	(0.4)	1	(0.4)	3	(0.4)
antiinflammatory and antirheumatic products	**128**	**(24.1)**	**64**	**(24.1)**	**192**	**(24.1)**
acemetacin	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) codeine phosphate (+) ibuprofen	3	(0.6)	0	(0.0)	3	(0.4)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
musculoskeletal system						
antiinflammatory and antirheumatic products	**128**	**(24.1)**	**64**	**(24.1)**	**192**	**(24.1)**
benzydamine hydrochloride	3	(0.6)	0	(0.0)	3	(0.4)
celecoxib	0	(0.0)	2	(0.8)	2	(0.3)
cetirizine hydrochloride (+) ibuprofen (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
chlorpheniramine maleate (+) ibuprofen (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
dexketoprofen	1	(0.2)	0	(0.0)	1	(0.1)
dexketoprofen tromethamine	0	(0.0)	1	(0.4)	1	(0.1)
diclofenac	10	(1.9)	7	(2.6)	17	(2.1)
diclofenac diethylamine	0	(0.0)	1	(0.4)	1	(0.1)
diclofenac potassium	1	(0.2)	2	(0.8)	3	(0.4)
diclofenac sodium	4	(0.8)	2	(0.8)	6	(0.8)
diphenhydramine citrate (+) ibuprofen	1	(0.2)	0	(0.0)	1	(0.1)
esomeprazole (+) meloxicam	1	(0.2)	0	(0.0)	1	(0.1)
etodolac	1	(0.2)	0	(0.0)	1	(0.1)
etoricoxib	3	(0.6)	1	(0.4)	4	(0.5)
flurbiprofen	1	(0.2)	0	(0.0)	1	(0.1)
ibuprofen	73	(13.7)	41	(15.4)	114	(14.3)
ibuprofen (+) pseudoephedrine hydrochloride	1	(0.2)	2	(0.8)	3	(0.4)
ibuprofen lysine	1	(0.2)	0	(0.0)	1	(0.1)
indomethacin	1	(0.2)	1	(0.4)	2	(0.3)
ketoprofen	7	(1.3)	1	(0.4)	8	(1.0)
ketorolac tromethamine	4	(0.8)	3	(1.1)	7	(0.9)
mefenamic acid	1	(0.2)	0	(0.0)	1	(0.1)
meloxicam	6	(1.1)	2	(0.8)	8	(1.0)
nabumetone	1	(0.2)	1	(0.4)	2	(0.3)
naproxen	16	(3.0)	4	(1.5)	20	(2.5)
naproxen sodium	7	(1.3)	2	(0.8)	9	(1.1)
nimesulide	1	(0.2)	1	(0.4)	2	(0.3)
oxaprozin	0	(0.0)	1	(0.4)	1	(0.1)
muscle relaxants	**23**	**(4.3)**	**8**	**(3.0)**	**31**	**(3.9)**
acetaminophen (+) chlorzoxazone	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) orphenadrine citrate	2	(0.4)	0	(0.0)	2	(0.3)
baclofen	1	(0.2)	0	(0.0)	1	(0.1)
chlormezanone	1	(0.2)	0	(0.0)	1	(0.1)
chlorzoxazone	0	(0.0)	1	(0.4)	1	(0.1)
cyclobenzaprine hydrochloride	9	(1.7)	2	(0.8)	11	(1.4)
diclofenac sodium (+) orphenadrine citrate	1	(0.2)	0	(0.0)	1	(0.1)
metaxalone	0	(0.0)	1	(0.4)	1	(0.1)
methocarbamol	6	(1.1)	0	(0.0)	6	(0.8)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
musculoskeletal system						
muscle relaxants	**23**	**(4.3)**	**8**	**(3.0)**	**31**	**(3.9)**
orphenadrine citrate	0	(0.0)	1	(0.4)	1	(0.1)
rocuronium bromide	1	(0.2)	0	(0.0)	1	(0.1)
succinylcholine chloride	1	(0.2)	0	(0.0)	1	(0.1)
thiocolchicoside	1	(0.2)	1	(0.4)	2	(0.3)
tizanidine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
tolperisone	1	(0.2)	2	(0.8)	3	(0.4)
other drugs for disorders of musculo-skeletal system	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
aminophylline (+) quinine sulfate	0	(0.0)	1	(0.4)	1	(0.1)
hyaluronic acid	1	(0.2)	0	(0.0)	1	(0.1)
topical products for joint and muscular pain	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.4)**
menthol (+) methyl salicylate	1	(0.2)	0	(0.0)	1	(0.1)
methyl salicylate	3	(0.6)	0	(0.0)	3	(0.4)
nervous system						
analgesics	**184**	**(34.7)**	**99**	**(37.2)**	**283**	**(35.5)**
acetaminophen	117	(22.0)	49	(18.4)	166	(20.8)
acetaminophen (+) ascorbic acid	1	(0.2)	1	(0.4)	2	(0.3)
acetaminophen (+) ascorbic acid (+) aspirin	2	(0.4)	0	(0.0)	2	(0.3)
acetaminophen (+) ascorbic acid (+) caffeine (+) chlorpheniramine maleate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) ascorbic acid (+) caffeine (+) phenylephrine hydrochloride (+) terpin hydrate	0	(0.0)	1	(0.4)	1	(0.1)
acetaminophen (+) aspirin (+) caffeine	3	(0.6)	5	(1.9)	8	(1.0)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) ephedrine hydrochloride	6	(1.1)	1	(0.4)	7	(0.9)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) phenylephrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
acetaminophen (+) caffeine (+) codeine phosphate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) caffeine (+) codeine phosphate (+) doxylamine succinate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) caffeine (+) codeine phosphate (+) meprobamate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) caffeine (+) opium	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) guaifenesin (+) phenylpropanolamine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
analgesics	**184**	**(34.7)**	**99**	**(37.2)**	**283**	**(35.5)**
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	1	(0.2)	3	(1.1)	4	(0.5)
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) pseudoephedrine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
acetaminophen (+) chlorpheniramine maleate (+) phenylephrine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
acetaminophen (+) chlorpheniramine maleate (+) phenylpropanolamine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
acetaminophen (+) chlorpheniramine maleate (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) codeine	2	(0.4)	2	(0.8)	4	(0.5)
acetaminophen (+) codeine phosphate	6	(1.1)	2	(0.8)	8	(1.0)
acetaminophen (+) codeine phosphate (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) codeine phosphate (+) phenylpropanolamine hydrochloride (+) phenyltoloxamine citrate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate	3	(0.6)	2	(0.8)	5	(0.6)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) ephedrine sulfate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	4	(0.8)	5	(1.9)	9	(1.1)
acetaminophen (+) dextromethorphan hydrobromide (+) promethazine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
acetaminophen (+) dextromethorphan hydrobromide (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) diphenhydramine hydrochloride (+) phenylephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) hydrocodone bitartrate	8	(1.5)	3	(1.1)	11	(1.4)
acetaminophen (+) ibuprofen	2	(0.4)	1	(0.4)	3	(0.4)
acetaminophen (+) oxycodone hydrochloride	7	(1.3)	3	(1.1)	10	(1.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
analgesics	**184**	**(34.7)**	**99**	**(37.2)**	**283**	**(35.5)**
acetaminophen (+) pheniramine maleate (+) phenylephrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
acetaminophen (+) phenylephrine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
acetaminophen (+) phenyltoloxamine citrate	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) pholcodine (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) pseudoephedrine hydrochloride	4	(0.8)	2	(0.8)	6	(0.8)
acetaminophen (+) sobrerol	1	(0.2)	0	(0.0)	1	(0.1)
acetaminophen (+) tramadol hydrochloride	3	(0.6)	2	(0.8)	5	(0.6)
anise oil (+) benzoic acid (+) camphor (+) licorice (+) opium	0	(0.0)	1	(0.4)	1	(0.1)
antimony potassium tartrate (+) benzoic acid (+) camphor (+) ethyl nitrite [spirit] (+) glycerin (+) licorice (+) opium	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) aspirin	2	(0.4)	0	(0.0)	2	(0.3)
aspirin	24	(4.5)	13	(4.9)	37	(4.6)
aspirin lysine	2	(0.4)	0	(0.0)	2	(0.3)
clonixin lysine	0	(0.0)	1	(0.4)	1	(0.1)
dihydrocodeine	0	(0.0)	2	(0.8)	2	(0.3)
dihydrocodeine bitartrate	0	(0.0)	1	(0.4)	1	(0.1)
dipyrone	8	(1.5)	6	(2.3)	14	(1.8)
eletriptan	0	(0.0)	1	(0.4)	1	(0.1)
eletriptan hydrobromide	0	(0.0)	1	(0.4)	1	(0.1)
fentanyl	2	(0.4)	0	(0.0)	2	(0.3)
fentanyl citrate	1	(0.2)	0	(0.0)	1	(0.1)
hydromorphone	3	(0.6)	0	(0.0)	3	(0.4)
hydromorphone hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
meperidine hydrochloride	1	(0.2)	3	(1.1)	4	(0.5)
morphine	4	(0.8)	1	(0.4)	5	(0.6)
morphine sulfate	2	(0.4)	0	(0.0)	2	(0.3)
naloxone hydrochloride (+) oxycodone hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
oxycodone	0	(0.0)	2	(0.8)	2	(0.3)
pizotyline malate	1	(0.2)	1	(0.4)	2	(0.3)
sumatriptan	1	(0.2)	1	(0.4)	2	(0.3)
tramadol hydrochloride	14	(2.6)	10	(3.8)	24	(3.0)
zolmitriptan	1	(0.2)	0	(0.0)	1	(0.1)
anesthetics	**14**	**(2.6)**	**3**	**(1.1)**	**17**	**(2.1)**
anesthetic (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
bupivacaine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
anesthetics	**14**	**(2.6)**	**3**	**(1.1)**	**17**	**(2.1)**
cocaine	1	(0.2)	0	(0.0)	1	(0.1)
epinephrine hydrochloride (+) lidocaine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
lidocaine	4	(0.8)	3	(1.1)	7	(0.9)
lidocaine hydrochloride	3	(0.6)	0	(0.0)	3	(0.4)
propofol	3	(0.6)	0	(0.0)	3	(0.4)
anti-Parkinson drugs	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
benztropine mesylate	1	(0.2)	1	(0.4)	2	(0.3)
biperiden hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
antiepileptics	**35**	**(6.6)**	**18**	**(6.8)**	**53**	**(6.6)**
carbamazepine	1	(0.2)	3	(1.1)	4	(0.5)
clonazepam	11	(2.1)	5	(1.9)	16	(2.0)
divalproex sodium	2	(0.4)	0	(0.0)	2	(0.3)
gabapentin	9	(1.7)	3	(1.1)	12	(1.5)
lamotrigine	1	(0.2)	2	(0.8)	3	(0.4)
levetiracetam	2	(0.4)	2	(0.8)	4	(0.5)
oxcarbazepine	0	(0.0)	1	(0.4)	1	(0.1)
pregabalin	7	(1.3)	3	(1.1)	10	(1.3)
primidone	1	(0.2)	0	(0.0)	1	(0.1)
topiramate	1	(0.2)	1	(0.4)	2	(0.3)
valproate sodium	3	(0.6)	2	(0.8)	5	(0.6)
valproic acid	1	(0.2)	0	(0.0)	1	(0.1)
other nervous system drugs	**14**	**(2.6)**	**6**	**(2.3)**	**20**	**(2.5)**
betahistine	0	(0.0)	1	(0.4)	1	(0.1)
betahistine hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
buprenorphine hydrochloride (+) naloxone hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
cinnarizine	0	(0.0)	1	(0.4)	1	(0.1)
methadone hydrochloride	4	(0.8)	0	(0.0)	4	(0.5)
nicotine	3	(0.6)	1	(0.4)	4	(0.5)
nicotine polacrilex	1	(0.2)	0	(0.0)	1	(0.1)
varenicline tartrate	5	(0.9)	2	(0.8)	7	(0.9)
psychoanaleptics	**66**	**(12.4)**	**41**	**(15.4)**	**107**	**(13.4)**
Asian ginseng (+) deanol tartrate (+) minerals (unspecified) (+) rutin (+) vitamins (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
acetylcarnitine	1	(0.2)	0	(0.0)	1	(0.1)
amitriptyline hydrochloride	13	(2.4)	2	(0.8)	15	(1.9)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
psychoanaleptics	**66**	**(12.4)**	**41**	**(15.4)**	**107**	**(13.4)**
amphetamine aspartate (+) amphetamine sulfate (+) dextroamphetamine saccharate (+) dextroamphetamine sulfate	5	(0.9)	4	(1.5)	9	(1.1)
bupropion hydrochloride	4	(0.8)	8	(3.0)	12	(1.5)
citalopram	6	(1.1)	1	(0.4)	7	(0.9)
citalopram hydrobromide	3	(0.6)	2	(0.8)	5	(0.6)
dextroamphetamine sulfate	1	(0.2)	0	(0.0)	1	(0.1)
dothiepin hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
duloxetine hydrochloride	4	(0.8)	3	(1.1)	7	(0.9)
escitalopram	3	(0.6)	1	(0.4)	4	(0.5)
escitalopram oxalate	8	(1.5)	5	(1.9)	13	(1.6)
fluoxetine	2	(0.4)	0	(0.0)	2	(0.3)
fluoxetine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
flupentixol hydrochloride (+) melitracen hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
fluvoxamine maleate	0	(0.0)	1	(0.4)	1	(0.1)
memantine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
methamphetamine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
methylenedioxymethamphetamine	1	(0.2)	0	(0.0)	1	(0.1)
methylphenidate hydrochloride	2	(0.4)	2	(0.8)	4	(0.5)
mianserin hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
mirtazapine	5	(0.9)	3	(1.1)	8	(1.0)
opipramol hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
oxitriptan	1	(0.2)	1	(0.4)	2	(0.3)
paroxetine	0	(0.0)	1	(0.4)	1	(0.1)
paroxetine hydrochloride	0	(0.0)	2	(0.8)	2	(0.3)
sertraline hydrochloride	11	(2.1)	8	(3.0)	19	(2.4)
trazodone hydrochloride	12	(2.3)	4	(1.5)	16	(2.0)
tryptophan	0	(0.0)	1	(0.4)	1	(0.1)
venlafaxine hydrochloride	4	(0.8)	2	(0.8)	6	(0.8)
vilazodone hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
vortioxetine hydrobromide	1	(0.2)	0	(0.0)	1	(0.1)
psycholeptics	**59**	**(11.1)**	**33**	**(12.4)**	**92**	**(11.5)**
European mistletoe (+) hops (+) lemon balm (+) St Johns wort (+) valerian (+) yarrow (+) yeast	1	(0.2)	0	(0.0)	1	(0.1)
alprazolam	13	(2.4)	4	(1.5)	17	(2.1)
aripiprazole	3	(0.6)	2	(0.8)	5	(0.6)
bromazepam	3	(0.6)	1	(0.4)	4	(0.5)
chlordiazepoxide hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
clobazam	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
nervous system						
psycholeptics	**59**	**(11.1)**	**33**	**(12.4)**	**92**	**(11.5)**
clothiapine	1	(0.2)	0	(0.0)	1	(0.1)
cloxazolam	1	(0.2)	0	(0.0)	1	(0.1)
diazepam	7	(1.3)	3	(1.1)	10	(1.3)
eszopiclone	1	(0.2)	0	(0.0)	1	(0.1)
ethyl loflazepate	2	(0.4)	0	(0.0)	2	(0.3)
etifoxine	1	(0.2)	0	(0.0)	1	(0.1)
flurazepam	1	(0.2)	0	(0.0)	1	(0.1)
haloperidol	2	(0.4)	1	(0.4)	3	(0.4)
hydroxyzine	2	(0.4)	0	(0.0)	2	(0.3)
hydroxyzine hydrochloride	4	(0.8)	1	(0.4)	5	(0.6)
hydroxyzine pamoate	1	(0.2)	1	(0.4)	2	(0.3)
levosulpiride	1	(0.2)	0	(0.0)	1	(0.1)
lithium	1	(0.2)	0	(0.0)	1	(0.1)
lithium carbonate	1	(0.2)	0	(0.0)	1	(0.1)
lorazepam	11	(2.1)	9	(3.4)	20	(2.5)
lormetazepam	0	(0.0)	1	(0.4)	1	(0.1)
lurasidone hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
mebutamate	1	(0.2)	0	(0.0)	1	(0.1)
melatonin	3	(0.6)	4	(1.5)	7	(0.9)
midazolam	2	(0.4)	1	(0.4)	3	(0.4)
olanzapine	0	(0.0)	1	(0.4)	1	(0.1)
prochlorperazine maleate	1	(0.2)	0	(0.0)	1	(0.1)
quetiapine fumarate	7	(1.3)	1	(0.4)	8	(1.0)
risperidone	2	(0.4)	0	(0.0)	2	(0.3)
sulpiride	0	(0.0)	1	(0.4)	1	(0.1)
suvorexant	1	(0.2)	0	(0.0)	1	(0.1)
temazepam	3	(0.6)	1	(0.4)	4	(0.5)
valerian	0	(0.0)	1	(0.4)	1	(0.1)
zolpidem	0	(0.0)	1	(0.4)	1	(0.1)
zolpidem tartrate	4	(0.8)	4	(1.5)	8	(1.0)
zopiclone	3	(0.6)	0	(0.0)	3	(0.4)
respiratory system						
antihistamines for systemic use	**87**	**(16.4)**	**30**	**(11.3)**	**117**	**(14.7)**
bilastine	2	(0.4)	0	(0.0)	2	(0.3)
cetirizine hydrochloride	21	(4.0)	10	(3.8)	31	(3.9)
chlorpheniramine	6	(1.1)	0	(0.0)	6	(0.8)
chlorpheniramine maleate	3	(0.6)	1	(0.4)	4	(0.5)
clemastine fumarate	1	(0.2)	0	(0.0)	1	(0.1)
cyclizine	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
respiratory system						
antihistamines for systemic use	**87**	**(16.4)**	**30**	**(11.3)**	**117**	**(14.7)**
cyclizine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
desloratadine	6	(1.1)	2	(0.8)	8	(1.0)
dexchlorpheniramine maleate	2	(0.4)	0	(0.0)	2	(0.3)
dimenhydrinate	3	(0.6)	2	(0.8)	5	(0.6)
diphenhydramine	4	(0.8)	2	(0.8)	6	(0.8)
diphenhydramine hydrochloride	7	(1.3)	5	(1.9)	12	(1.5)
doxylamine succinate	0	(0.0)	1	(0.4)	1	(0.1)
ebastine	8	(1.5)	0	(0.0)	8	(1.0)
fexofenadine hydrochloride	2	(0.4)	2	(0.8)	4	(0.5)
ketotifen fumarate	1	(0.2)	1	(0.4)	2	(0.3)
levocetirizine	2	(0.4)	0	(0.0)	2	(0.3)
levocetirizine dihydrochloride	3	(0.6)	3	(1.1)	6	(0.8)
loratadine	25	(4.7)	5	(1.9)	30	(3.8)
meclizine	0	(0.0)	1	(0.4)	1	(0.1)
oxomemazine	1	(0.2)	0	(0.0)	1	(0.1)
promethazine	3	(0.6)	0	(0.0)	3	(0.4)
promethazine hydrochloride	4	(0.8)	1	(0.4)	5	(0.6)
rupatadine	1	(0.2)	0	(0.0)	1	(0.1)
cough and cold preparations	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
Indian squill (+) ipecac (+) licorice	0	(0.0)	1	(0.4)	1	(0.1)
acetylcysteine	3	(0.6)	4	(1.5)	7	(0.9)
ambroxol	2	(0.4)	0	(0.0)	2	(0.3)
ambroxol hydrochloride	1	(0.2)	1	(0.4)	2	(0.3)
ambroxol hydrochloride (+) clenbuterol hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
ammonium chloride (+) buchu (+) camphor (+) olive oil (+) red cinchona (+) Seneca snakeroot (+) sulfur (+) turpentine (+) Virginia snakeroot	1	(0.2)	0	(0.0)	1	(0.1)
ammonium chloride (+) dextromethorphan hydrobromide (+) sodium citrate	0	(0.0)	1	(0.4)	1	(0.1)
ammonium chloride (+) diphenhydramine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
ammonium chloride (+) diphenhydramine hydrochloride (+) sodium citrate	0	(0.0)	1	(0.4)	1	(0.1)
benzonatate	1	(0.2)	3	(1.1)	4	(0.5)
black cherry (+) ipecac (+) licorice (+) squill (+) tolu balsam	0	(0.0)	1	(0.4)	1	(0.1)
bromhexine hydrochloride	3	(0.6)	3	(1.1)	6	(0.8)
carbocysteine	1	(0.2)	3	(1.1)	4	(0.5)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
respiratory system						
cough and cold preparations	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
chlorpheniramine maleate (+) codeine phosphate (+) pseudoephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
chlorpheniramine maleate (+) hydrocodone bitartrate	0	(0.0)	1	(0.4)	1	(0.1)
codeine	2	(0.4)	1	(0.4)	3	(0.4)
codeine (+) guaifenesin	0	(0.0)	1	(0.4)	1	(0.1)
codeine phosphate	0	(0.0)	1	(0.4)	1	(0.1)
codeine phosphate (+) promethazine hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
cough, cold, and flu therapies (unspecified)	5	(0.9)	4	(1.5)	9	(1.1)
dextromethorphan	2	(0.4)	2	(0.8)	4	(0.5)
dextromethorphan hydrobromide	2	(0.4)	0	(0.0)	2	(0.3)
dextromethorphan hydrobromide (+) guaifenesin	2	(0.4)	0	(0.0)	2	(0.3)
guaifenesin	7	(1.3)	1	(0.4)	8	(1.0)
hydrocodone	0	(0.0)	1	(0.4)	1	(0.1)
levodropropizine	1	(0.2)	0	(0.0)	1	(0.1)
potassium iodide	1	(0.2)	0	(0.0)	1	(0.1)
drugs for obstructive airway diseases	**36**	**(6.8)**	**26**	**(9.8)**	**62**	**(7.8)**
aclidinium bromide	1	(0.2)	0	(0.0)	1	(0.1)
albuterol	12	(2.3)	7	(2.6)	19	(2.4)
albuterol sulfate	5	(0.9)	5	(1.9)	10	(1.3)
albuterol sulfate (+) beclomethasone dipropionate	0	(0.0)	1	(0.4)	1	(0.1)
albuterol sulfate (+) ipratropium bromide	1	(0.2)	0	(0.0)	1	(0.1)
ammonium chloride (+) diphenylpyraline hydrochloride (+) etofylline (+) sodium citrate (+) theophylline	1	(0.2)	0	(0.0)	1	(0.1)
arformoterol tartrate	0	(0.0)	1	(0.4)	1	(0.1)
beclomethasone dipropionate	5	(0.9)	1	(0.4)	6	(0.8)
beclomethasone dipropionate (+) formoterol fumarate	1	(0.2)	0	(0.0)	1	(0.1)
budesonide	0	(0.0)	2	(0.8)	2	(0.3)
budesonide (+) formoterol fumarate	3	(0.6)	1	(0.4)	4	(0.5)
ciclesonide	2	(0.4)	2	(0.8)	4	(0.5)
cromolyn sodium	1	(0.2)	1	(0.4)	2	(0.3)
epinephrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
fenoterol hydrobromide (+) ipratropium bromide	1	(0.2)	0	(0.0)	1	(0.1)
fluticasone	5	(0.9)	0	(0.0)	5	(0.6)
fluticasone furoate	3	(0.6)	1	(0.4)	4	(0.5)
fluticasone furoate (+) vilanterol trifenatate	1	(0.2)	0	(0.0)	1	(0.1)
fluticasone propionate	3	(0.6)	6	(2.3)	9	(1.1)
fluticasone propionate (+) salmeterol xinafoate	1	(0.2)	2	(0.8)	3	(0.4)

Subjects With Specific Concomitant Medications
(Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
respiratory system						
drugs for obstructive airway diseases	**36**	**(6.8)**	**26**	**(9.8)**	**62**	**(7.8)**
formoterol fumarate	1	(0.2)	0	(0.0)	1	(0.1)
ipratropium bromide	2	(0.4)	1	(0.4)	3	(0.4)
montelukast	2	(0.4)	0	(0.0)	2	(0.3)
montelukast sodium	1	(0.2)	0	(0.0)	1	(0.1)
salmeterol	1	(0.2)	0	(0.0)	1	(0.1)
terbutaline sulfate	0	(0.0)	2	(0.8)	2	(0.3)
vilanterol	1	(0.2)	0	(0.0)	1	(0.1)
nasal preparations	**16**	**(3.0)**	**16**	**(6.0)**	**32**	**(4.0)**
acetylcysteine (+) tuaminoheptane sulfate	0	(0.0)	2	(0.8)	2	(0.3)
azelastine hydrochloride (+) fluticasone propionate	0	(0.0)	1	(0.4)	1	(0.1)
benzocaine (+) ephedrine hydrochloride	1	(0.2)	0	(0.0)	1	(0.1)
camphor (+) eucalyptus oil (+) menthol (+) thymol	1	(0.2)	0	(0.0)	1	(0.1)
cetirizine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
chlorpheniramine maleate (+) phenylephrine hydrochloride (+) phenylpropanolamine hydrochloride (+) phenyltoloxamine citrate	1	(0.2)	0	(0.0)	1	(0.1)
dexamethasone isonicotinate (+) neomycin sulfate (+) tramazoline hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
diphenylpyraline hydrochloride (+) phenylephrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
fexofenadine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
loratadine (+) pseudoephedrine sulfate	3	(0.6)	1	(0.4)	4	(0.5)
naphazoline hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
oxymetazoline hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
phenylephrine	2	(0.4)	0	(0.0)	2	(0.3)
pseudoephedrine	0	(0.0)	2	(0.8)	2	(0.3)
pseudoephedrine hydrochloride	3	(0.6)	1	(0.4)	4	(0.5)
tetrahydrozoline hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
tixocortol pivalate	0	(0.0)	1	(0.4)	1	(0.1)
xylometazoline hydrochloride	4	(0.8)	4	(1.5)	8	(1.0)
other respiratory system products	**0**	**(0.0)**	**2**	**(0.8)**	**2**	**(0.3)**
eucalyptus oil (+) menthol	0	(0.0)	1	(0.4)	1	(0.1)
menthol	0	(0.0)	1	(0.4)	1	(0.1)
throat preparations	**5**	**(0.9)**	**1**	**(0.4)**	**6**	**(0.8)**
amylmetacresol (+) dichlorobenzyl alcohol	1	(0.2)	1	(0.4)	2	(0.3)
benzocaine (+) cetylpyridinium chloride	2	(0.4)	0	(0.0)	2	(0.3)
fusafungine	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
sensory organs						
ophthalmological and otological preparations	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
dexamethasone (+) gentamicin sulfate	1	(0.2)	0	(0.0)	1	(0.1)
dexamethasone sodium phosphate (+) neomycin sulfate (+) polymyxin B sulfate	0	(0.0)	1	(0.4)	1	(0.1)
hydrocortisone (+) neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
ophthalmologicals	**10**	**(1.9)**	**2**	**(0.8)**	**12**	**(1.5)**
antazoline hydrochloride (+) tetrahydrozoline hydrochloride	2	(0.4)	0	(0.0)	2	(0.3)
brimonidine tartrate (+) timolol maleate	1	(0.2)	0	(0.0)	1	(0.1)
carboxymethylcellulose sodium	1	(0.2)	0	(0.0)	1	(0.1)
ciprofloxacin hydrochloride (+) dexamethasone	1	(0.2)	0	(0.0)	1	(0.1)
dexamethasone (+) tobramycin	0	(0.0)	2	(0.8)	2	(0.3)
dextran 70 (+) hypromellose	2	(0.4)	0	(0.0)	2	(0.3)
gramicidin (+) neomycin sulfate (+) polymyxin B sulfate	1	(0.2)	0	(0.0)	1	(0.1)
hydrocortisone acetate (+) neomycin sulfate	1	(0.2)	0	(0.0)	1	(0.1)
isospaglumic acid (+) spaglumic acid	1	(0.2)	0	(0.0)	1	(0.1)
lanolin (+) mineral oil (+) petrolatum, white	1	(0.2)	0	(0.0)	1	(0.1)
nepafenac	0	(0.0)	1	(0.4)	1	(0.1)
otologicals	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
antipyrine (+) benzocaine (+) glycerin	1	(0.2)	1	(0.4)	2	(0.3)
systemic hormonal preparations, excl. sex hormones and insulins						
corticosteroids for systemic use	**43**	**(8.1)**	**25**	**(9.4)**	**68**	**(8.5)**
betamethasone	3	(0.6)	3	(1.1)	6	(0.8)
betamethasone sodium phosphate	0	(0.0)	1	(0.4)	1	(0.1)
corticosteroids (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
cortisone	0	(0.0)	2	(0.8)	2	(0.3)
dexamethasone	2	(0.4)	3	(1.1)	5	(0.6)
hydrocortisone	5	(0.9)	2	(0.8)	7	(0.9)
methylprednisolone	5	(0.9)	3	(1.1)	8	(1.0)
methylprednisolone acetate	1	(0.2)	0	(0.0)	1	(0.1)
methylprednisolone sodium succinate	1	(0.2)	0	(0.0)	1	(0.1)
prednisolone	9	(1.7)	2	(0.8)	11	(1.4)
prednisolone acetate	0	(0.0)	1	(0.4)	1	(0.1)
prednisolone sodium succinate	1	(0.2)	0	(0.0)	1	(0.1)
prednisone	7	(1.3)	6	(2.3)	13	(1.6)
triamcinolone	7	(1.3)	2	(0.8)	9	(1.1)
triamcinolone acetonide	5	(0.9)	4	(1.5)	9	(1.1)
thyroid therapy	**4**	**(0.8)**	**4**	**(1.5)**	**8**	**(1.0)**

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
systemic hormonal preparations, excl. sex hormones and insulins						
thyroid therapy	**4**	**(0.8)**	**4**	**(1.5)**	**8**	**(1.0)**
levothyroxine sodium	4	(0.8)	4	(1.5)	8	(1.0)
various						
all other therapeutic products	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
Aphanizomenon flosaquae (+) bilberry (+) blueberry (+) caffeine (+) chlorella (+) chocolate (+) cranberry (+) damiana (+) Fragaria virginiana (+) grape (+) grape seeds (+) guarana (+) mate (+) plum (+) raspberry (+) rice (+) sour cherry	0	(0.0)	1	(0.4)	1	(0.1)
Asian ginseng (+) amino acids (+) aminobenzoic acid (+) bovine colostrum (+) bovine liver (+) coenzyme A (+) conductase (+) eleuthero (+) inosine (+) minerals (+) phosphatidyl choline (+) sarsaparilla (+) shark cartilage (+) thioctic acid (+) vitamins	1	(0.2)	0	(0.0)	1	(0.1)
CT-102 activated platelet supernatant	1	(0.2)	0	(0.0)	1	(0.1)
Candida albicans (+) Haemophilus influenzae lysate (+) Neisseria catarrhalis lysate (+) Staphylococcus albus lysate (+) Staphylococcus aureus (+) Streptococcus haemolyticus lysate (+) Streptococcus pneumoniae lysate (+) Streptococcus viridans lysate	0	(0.0)	1	(0.4)	1	(0.1)
Chinese skullcap (+) coptis (+) dandelion (+) gardenia (+) isatis (+) Japanese honeysuckle (+) knotweed (+) shrubby sophora (+) sweet wormwood (+) Tokyo violet (+) wild chrysanthemum	1	(0.2)	0	(0.0)	1	(0.1)
Pelargonium sidoides	1	(0.2)	0	(0.0)	1	(0.1)
Plantago arenaria	0	(0.0)	1	(0.4)	1	(0.1)
[composition unspecified]	3	(0.6)	1	(0.4)	4	(0.5)
acetyl tyrosine (+) acetylcarnitine (+) caffeine (+) cyanocobalamin (+) folic acid (+) glucurolactone (+) malic acid (+) niacinamide (+) pantothenic acid (+) phenylalanine (+) pyridoxine hydrochloride (+) taurine	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
acetyl tyrosine (+) alpha-yohimbe (+) arginine (+) arginine ketoglutarate(+) beta alanine (+) caffeine (+) calcium fructoborate (+) citrulline (+) deanol (+) pterostilbene (+) resveratrol (+) theanine	1	(0.2)	0	(0.0)	1	(0.1)
acetylcysteine (+) arginine hydrochloride (+) glutamine (+) lysine hydrochloride (+) pidolic acid (+) schizonepeta	0	(0.0)	1	(0.4)	1	(0.1)
ajowan (+) anise (+) ascorbic acid (+) cinnamon (+) eucalyptus (+) fenugreek (+) garden daisy (+) grape (+) lemon (+) lesser galangal (+) mullein (+) oat (+) plantain (+) sage (+) thyme (+) turmeric	1	(0.2)	0	(0.0)	1	(0.1)
alcohol	1	(0.2)	0	(0.0)	1	(0.1)
alfalfa (+) algae (+) amla (+) chocolate (+) coffee (+) eleuthero (+) fiber (+) fruit (+) ginkgo (+) grains (+) licorice (+) milk thistle (+) nigella (+) purslane (+) resveratrol (+) sea buckthorn (+) sunflower (+) tea (+) vegetables (+) xanthophyll	0	(0.0)	1	(0.4)	1	(0.1)
ammonium chloride (+) belleric myrobalan (+) Clerodenrum serratum (+) Elephantopus scaber (+) ephedra (+) herbs (+) holy basil (+) horn of plenty (+) jatamansi (+) Malabar nut tree (+) pepper (+) spiked ginger lily (+) turmeric (+) yellow fruit nightshade	0	(0.0)	1	(0.4)	1	(0.1)
andrographis (+) dandelion (+) Japanese honeysuckle	1	(0.2)	0	(0.0)	1	(0.1)
anthocyanins (unspecified) (+) beta alanine (+) citrulline (+) creatine (+) rhodiola (+) schisandra (+) yohimbe	1	(0.2)	0	(0.0)	1	(0.1)
antioxidants (+) ashwagandha (+) astragalus (+) dandelion (+) digestive enzymes (+) eleuthero (+) fruit (+) ginger (+) ginkgo (+) hawthorn (+) minerals (+) oregano (+) saw palmetto (+) schisandra (+) shiitake (+) stinging nettle (+) turmeric (+) vitamins	0	(0.0)	1	(0.4)	1	(0.1)
arginine ketoglutarate (+) beta alanine (+) caffeine (+) creatine (+) methylhexaneamine (+) schisandra	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
artichoke (+) calcium phosphate, dibasic (+) milk thistle (+) riboflavin (+) turmeric	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) Bacillus coagulans (+) butchers broom	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) bergamot orange	1	(0.2)	0	(0.0)	1	(0.1)
ascorbic acid (+) chondroitin sulfate sodium (+) collagen (+) glucosamine sulfate	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) chondroitin sulfate sodium (+) dimethyl sulfone (+) gelatin (+) glucosamine hydrochloride (+) hyaluronic acid (+) Indian frankincense (+) manganese sulfate (+) sodium borate	0	(0.0)	1	(0.4)	1	(0.1)
ascorbic acid (+) dimethyl sulfone (+) ginger (+) glucosamine sulfate (+) manganese sulfate (+) white willow	1	(0.2)	0	(0.0)	1	(0.1)
ashwagandha (+) calcium phosphate, dibasic (+) cholecalciferol (+) chromium picolinate (+) cordyceps (+) diindolylmethane (+) mecobalamin (+) piperine (+) pyridoxine hydrochloride (+) zinc methionine	1	(0.2)	0	(0.0)	1	(0.1)
astragalus (+) bai zhu atractylodes (+) bupleurum (+) chebulic myrobalan (+) Chinese cimicifuga (+) Chinese licorice (+) codonopsis (+) dong quai (+) magnolia (+) plantago seed (+) schisandra (+) schizonepeta (+) Sichuan lovage (+) siler (+) xanthium	1	(0.2)	0	(0.0)	1	(0.1)
astragalus (+) bovine colostrum (+) grapefruit (+) maitake (+) reishi (+) shiitake (+) propolis	1	(0.2)	0	(0.0)	1	(0.1)
astragalus (+) cleavers (+) dandelion (+) European elder (+) milk thistle (+) propolis (+) wild indigo	0	(0.0)	1	(0.4)	1	(0.1)
balloon vine (+) chaparral (+) Galphimia glauca (+) khella (+) Luffa operculata (+) spikenard	1	(0.2)	0	(0.0)	1	(0.1)
betaine (+) creatine (+) creatine hydrochloride (+) dextrose (+) glutamine (+) glycine (+) isoleucine (+) leucine (+) potassium phosphate, dibasic (+) sodium phosphate, dibasic (+) taurine (+) valine	0	(0.0)	1	(0.4)	1	(0.1)
biotin (+) black currant (+) borage oil (+) cysteine (+) sodium selenite (+) zinc sulfate	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
bismuth	0	(0.0)	1	(0.4)	1	(0.1)
boldo	1	(0.2)	0	(0.0)	1	(0.1)
caffeine (+) capsicum (+) catechu (+) damiana (+) guarana (+) mate (+) velvet bean	0	(0.0)	1	(0.4)	1	(0.1)
calcium phosphate, tribasic (+) carbohydrates (+) chromium polynicotinate (+) conductase (+) creatine (+) glutamine (+) glutathione (+) magnesium citrate (+) potassium chloride (+) potassium citrate (+) sodium citrate (+) ubidecarenone (+) vitamins	0	(0.0)	1	(0.4)	1	(0.1)
carbon black	0	(0.0)	1	(0.4)	1	(0.1)
cholecalciferol (+) lactoferrin (as drug) (+) zinc oxide	0	(0.0)	1	(0.4)	1	(0.1)
chondroitin sulfate sodium (+) dimethyl sulfone (+) glucosamine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
chondroitin sulfate sodium (+) glucosamine sulfate	2	(0.4)	0	(0.0)	2	(0.3)
cranberry	1	(0.2)	1	(0.4)	2	(0.3)
dimethyl sulfone	1	(0.2)	0	(0.0)	1	(0.1)
dimethyl sulfone (+) glucosamine hydrochloride	0	(0.0)	1	(0.4)	1	(0.1)
echinacea (unspecified)	1	(0.2)	2	(0.8)	3	(0.4)
escin	1	(0.2)	0	(0.0)	1	(0.1)
eucalyptus oil (+) fir oil (+) mallow (+) mullein (+) myrtle oil (+) pine oil (+) thyme oil	1	(0.2)	0	(0.0)	1	(0.1)
eupatilin	1	(0.2)	0	(0.0)	1	(0.1)
folinic acid	1	(0.2)	0	(0.0)	1	(0.1)
fulvic acid (+) glutamine (+) selenium (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
ginseng (unspecified)	2	(0.4)	0	(0.0)	2	(0.3)
glucosamine	0	(0.0)	1	(0.4)	1	(0.1)
hemp	2	(0.4)	1	(0.4)	3	(0.4)
herbs (unspecified)	1	(0.2)	0	(0.0)	1	(0.1)
ichthyo liver oil	1	(0.2)	0	(0.0)	1	(0.1)
lemon balm	0	(0.0)	1	(0.4)	1	(0.1)
leucovorin calcium	0	(0.0)	3	(1.1)	3	(0.4)
nitrogen	2	(0.4)	1	(0.4)	3	(0.4)
oregano oil	0	(0.0)	1	(0.4)	1	(0.1)
prasterone	1	(0.2)	1	(0.4)	2	(0.3)
propolis	1	(0.2)	0	(0.0)	1	(0.1)
royal jelly	1	(0.2)	0	(0.0)	1	(0.1)
saw palmetto	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
various						
all other therapeutic products	**34**	**(6.4)**	**25**	**(9.4)**	**59**	**(7.4)**
serum-derived bovine immunoglobulin/protein isolate	1	(0.2)	0	(0.0)	1	(0.1)
spirulina	1	(0.2)	1	(0.4)	2	(0.3)
trichloroacetic acid	0	(0.0)	1	(0.4)	1	(0.1)
allergens	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
allergenic extract (+) echinacea (unspecified) (+) fenugreek (+) goldenseal (+) myrrh (+) poke (+) watercress (+) wild indigo	0	(0.0)	1	(0.4)	1	(0.1)
contrast media	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
iohexol	1	(0.2)	0	(0.0)	1	(0.1)
diagnostic agents	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
tuberculin purified protein derivative	0	(0.0)	1	(0.4)	1	(0.1)
general nutrients	**4**	**(0.8)**	**7**	**(2.6)**	**11**	**(1.4)**
amino acids (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
creatine	0	(0.0)	2	(0.8)	2	(0.3)
creatine (+) glutamine (+) isoleucine (+) lecithin (+) leucine (+) protein (unspecified) (+) taurine (+) valine	0	(0.0)	1	(0.4)	1	(0.1)
creatine (+) protein (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
lecithin	0	(0.0)	1	(0.4)	1	(0.1)
minerals (unspecified) (+) protein (unspecified) (+) vitamins (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
nutritional supplements	0	(0.0)	1	(0.4)	1	(0.1)
protease (+) protein (unspecified)	0	(0.0)	1	(0.4)	1	(0.1)
protein (unspecified)	4	(0.8)	1	(0.4)	5	(0.6)

Every subject is counted a single time for each applicable specific concomitant medication. A subject with multiple concomitant medications within a medication category is counted a single time for that category.

A medication class or specific medication appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 11

Summary of Subject Compliance With Study Therapy
Primary Compliance
Weeks 0-48

	Raltegravir 1200 mg QD n (%)	Raltegravir 400 mg BID n (%)	Total n (%)
Subjects in population	531	266	797
Percent compliance†			
100%	377 (71.0)	189 (71.1)	566 (71.0)
99 to 90%	139 (26.2)	66 (24.8)	205 (25.7)
89 to 80%	7 (1.3)	10 (3.8)	17 (2.1)
79 to 70%	3 (0.6)	1 (0.4)	4 (0.5)
<70%	5 (0.9)	0 (0.0)	5 (0.6)
Summary statistics for treatment compliance			
Days in Study			
Mean (SD)	353.6 (67.01)	352.6 (69.57)	353.3 (67.83)
Median	378	378	378
Range	9 - 378	7 - 378	7 - 378
Days on Study Therapy			
Mean (SD)	349.9 (69.99)	349.0 (70.81)	349.6 (70.22)
Median	378	378	378
Range	9 - 378	7 - 378	7 - 378

†Percent compliance:[number of days on therapy / number of days should be on therapy] * 100. A day within the study is considered an "On-Therapy" day if the subject takes at least one tablet from any bottle provided for this study.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 12

Summary of Subject Compliance With Study Therapy
Full Compliance
Weeks 0-48

	Raltegravir 1200 mg QD n (%)	Raltegravir 400 mg BID n (%)	Total n (%)
Subjects in population	531	266	797
Percent compliance†			
100%	252 (47.5)	125 (47.0)	377 (47.3)
99 to 90%	244 (46.0)	118 (44.4)	362 (45.4)
89 to 80%	21 (4.0)	14 (5.3)	35 (4.4)
79 to 70%	8 (1.5)	6 (2.3)	14 (1.8)
<70%	6 (1.1)	3 (1.1)	9 (1.1)
Summary statistics for treatment compliance			
Days in Study			
Mean (SD)	353.6 (67.01)	352.6 (69.57)	353.3 (67.83)
Median	378	378	378
Range	9 - 378	7 - 378	7 - 378
Days on Study Therapy			
Mean (SD)	346.3 (70.63)	345.1 (71.71)	345.9 (70.95)
Median	376	376	376
Range	9 - 378	6 - 378	6 - 378

†Percent compliance:[number of days on therapy / number of days should be on therapy] * 100. A day within the study is considered an "On-Therapy" day if the subject takes the required number of tablets from all bottles provided for this study.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 13

Proportion of Subjects with HIV RNA <40 copies/mL Over Time
Observed Failure Approach

Endpoint	Visit	Response				Treatment Difference (QD – BID)†	
		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference	95% CI
		n/N	% (95% CI)	n/N	% (95% CI)		
Proportions with HIV RNA <40 copies/mL	Week 4	284/523	54.3 (49.9, 58.6)	138/261	52.9 (46.6, 59.1)	1.0	(-5.4, 7.4)
	Week 8	405/518	78.2 (74.4, 81.7)	208/259	80.3 (74.9, 85.0)	-2.4	(-7.8, 2.9)
	Week 16	436/512	85.2 (81.8, 88.1)	222/259	85.7 (80.9, 89.7)	-0.6	(-5.5, 4.3)
	Week 24	464/514	90.3 (87.4, 92.7)	230/257	89.5 (85.1, 93.0)	0.7	(-3.7, 5.2)
	Week 36	463/501	92.4 (89.7, 94.6)	236/254	92.9 (89.0, 95.7)	-0.6	(-4.5, 3.4)
	Week 48	472/501	94.2 (91.8, 96.1)	235/251	93.6 (89.9, 96.3)	0.6	(-3.1, 4.2)

Approach to handling missing values: Observed Failure Approach under which missing values for subjects who discontinued assigned therapy due to lack of efficacy was counted as failure.

†A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs for the treatment differences in percent response were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA <=100,000 copies/mL or HIV-1 RNA >100,000 copies/mL).

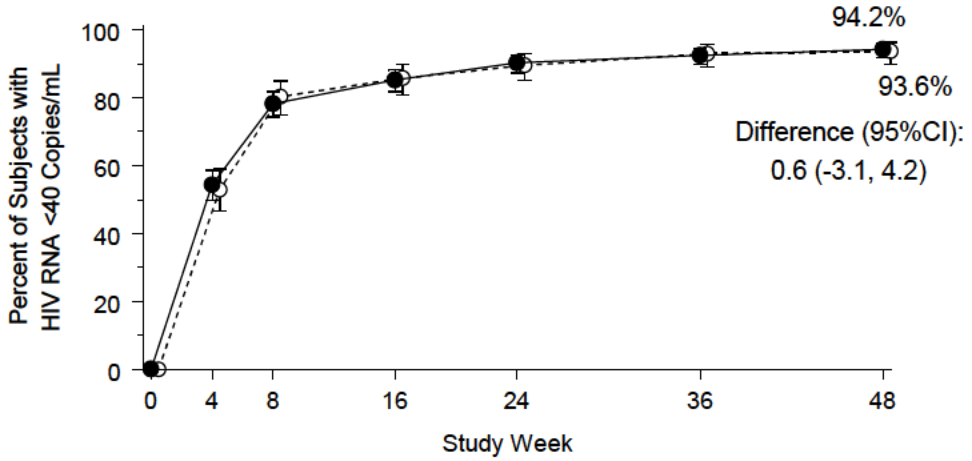
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 1

Proportion of Subjects With HIV RNA < 40 copies/mL Over Time (95% CI)
Observed Failure Approach



Number of Contributing Patients

● RAL 1200 mg QD	531	523	518	512	514	501	501
○ RAL 400 mg BID	266	261	259	259	257	254	251

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 14

Proportion of Subjects with HIV RNA <50 copies/mL Over Time
FDA Snapshot Approach (Non-Completer = Failure)

Endpoint	Visit	Response				Treatment Difference (QD – BID)†	
		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference	95% CI
		n/N	% (95% CI)	n/N	% (95% CI)		
Proportions with HIV RNA <50 copies/mL	Week 4	310/531	58.4 (54.1, 62.6)	153/266	57.5 (51.3, 63.5)	0.6	(-5.7, 6.9)
	Week 8	430/531	81.0 (77.4, 84.2)	219/266	82.3 (77.2, 86.7)	-1.5	(-6.7, 3.6)
	Week 16	455/531	85.7 (82.4, 88.6)	234/266	88.0 (83.4, 91.6)	-2.4	(-7.1, 2.3)
	Week 24	475/531	89.5 (86.5, 91.9)	233/266	87.6 (83.0, 91.3)	1.8	(-2.9, 6.5)
	Week 36	472/531	88.9 (85.9, 91.4)	242/266	91.0 (86.9, 94.1)	-2.1	(-6.5, 2.3)
	Week 48	477/531	89.8 (86.9, 92.3)	240/266	90.2 (86.0, 93.5)	-0.4	(-4.9, 4.0)

Approach to handling missing values: Non-Completer = Failure (NC=F) Approach as defined by FDA snapshot approach under which all missing values were counted as failure.

†A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs for the treatment differences in percent response were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA <=100,000 copies/mL or HIV-1 RNA >100,000 copies/mL).

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 15

Proportion of Subjects with HIV RNA <50 copies/mL Over Time
Observed Failure Approach

Endpoint	Visit	Response				Treatment Difference (QD – BID)†	
		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference	95% CI
		n/N	% (95% CI)	n/N	% (95% CI)		
Proportions with HIV RNA <50 copies/mL	Week 4	310/523	59.3 (54.9, 63.5)	153/261	58.6 (52.4, 64.7)	0.2	(-6.1, 6.5)
	Week 8	430/518	83.0 (79.5, 86.1)	219/259	84.6 (79.6, 88.7)	-1.8	(-6.7, 3.0)
	Week 16	455/512	88.9 (85.8, 91.5)	234/259	90.3 (86.1, 93.7)	-1.5	(-5.8, 2.8)
	Week 24	475/514	92.4 (89.8, 94.5)	233/257	90.7 (86.4, 93.9)	1.7	(-2.5, 5.9)
	Week 36	472/501	94.2 (91.8, 96.1)	242/254	95.3 (91.9, 97.5)	-1.1	(-4.5, 2.3)
	Week 48	477/501	95.2 (93.0, 96.9)	240/251	95.6 (92.3, 97.8)	-0.4	(-3.6, 2.8)

Approach to handling missing values: Observed Failure Approach under which missing values for subjects who discontinued assigned therapy due to lack of efficacy was counted as failure.

†A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs for the treatment differences in percent response were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA <=100,000 copies/mL or HIV-1 RNA >100,000 copies/mL).

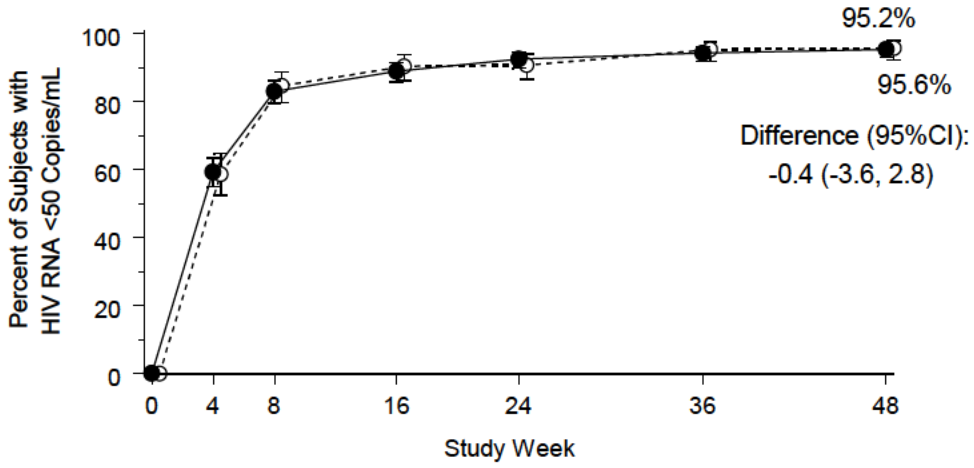
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 2

Proportion of Subjects With HIV RNA < 50 copies/mL Over Time (95% CI)
Observed Failure Approach



Number of Contributing Patients

● RAL 1200 mg QD	531	523	518	512	514	501	501
○ RAL 400 mg BID	266	261	259	259	257	254	251

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 16

Proportion of Subjects with HIV RNA <200 copies/mL Over Time
FDA Snapshot Approach (Non-Completer = Failure)

Endpoint	Visit	Response				Treatment Difference (QD – BID)†	
		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference	95% CI
		n/N	% (95% CI)	n/N	% (95% CI)		
Proportions with HIV RNA <200 copies/mL	Week 4	470/531	88.5 (85.5, 91.1)	229/266	86.1 (81.3, 90.0)	2.3	(-2.3, 6.9)
	Week 8	497/531	93.6 (91.2, 95.5)	250/266	94.0 (90.4, 96.5)	-0.4	(-4.0, 3.1)
	Week 16	501/531	94.4 (92.0, 96.2)	254/266	95.5 (92.3, 97.6)	-1.2	(-4.4, 2.1)
	Week 24	500/531	94.2 (91.8, 96.0)	248/266	93.2 (89.5, 95.9)	0.9	(-2.8, 4.6)
	Week 36	488/531	91.9 (89.2, 94.1)	247/266	92.9 (89.1, 95.6)	-1.0	(-4.9, 3.0)
	Week 48	484/531	91.1 (88.4, 93.4)	243/266	91.4 (87.3, 94.4)	-0.2	(-4.4, 4.0)

Approach to handling missing values: Non-Completer = Failure (NC=F) Approach as defined by FDA snapshot approach under which all missing values were counted as failure.

†A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs for the treatment differences in percent response were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA <=100,000 copies/mL or HIV-1 RNA >100,000 copies/mL).

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 17

Proportion of Subjects with HIV RNA <200 copies/mL Over Time
Observed Failure Approach

Endpoint	Visit	Response				Treatment Difference (QD – BID)†	
		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference	95% CI
		n/N	% (95% CI)	n/N	% (95% CI)		
Proportions with HIV RNA <200 copies/mL	Week 4	470/523	89.9 (87.0, 92.3)	229/261	87.7 (83.1, 91.5)	1.9	(-2.5, 6.3)
	Week 8	497/518	95.9 (93.9, 97.5)	250/259	96.5 (93.5, 98.4)	-0.7	(-3.5, 2.1)
	Week 16	501/512	97.9 (96.2, 98.9)	254/259	98.1 (95.6, 99.4)	-0.2	(-2.4, 2.0)
	Week 24	500/514	97.3 (95.5, 98.5)	248/257	96.5 (93.5, 98.4)	0.8	(-2.0, 3.5)
	Week 36	488/501	97.4 (95.6, 98.6)	247/254	97.2 (94.4, 98.9)	0.1	(-2.4, 2.7)
	Week 48	484/501	96.6 (94.6, 98.0)	243/251	96.8 (93.8, 98.6)	-0.2	(-3.0, 2.6)

Approach to handling missing values: Observed Failure Approach under which missing values for subjects who discontinued assigned therapy due to lack of efficacy was counted as failure.

†A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs for the treatment differences in percent response were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA <=100,000 copies/mL or HIV-1 RNA >100,000 copies/mL).

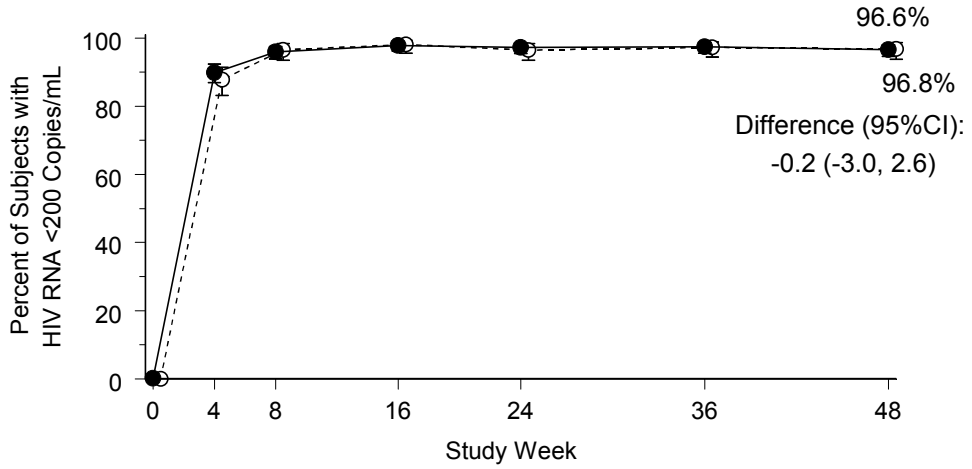
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 3

Proportion of Subjects With HIV RNA < 200 copies/mL Over Time (95% CI)
Observed Failure Approach



Number of Contributing Patients

● RAL 1200 mg QD	531	523	518	512	514	501	501
○ RAL 400 mg BID	266	261	259	259	257	254	251

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 18

Proportion of Subjects with HIV RNA in Various Categories Over Time
Data as Observed

Visit	Treatment Group	Viral Load Category						
		<40 copies/mL Target Not Detected	<40 copies/mL Target Detected	40 - <50 copies/mL	50 - <100 copies/mL	100 - <200 copies/mL	>200 copies/mL	Missing
		n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)	n/N (%)
Week 4	Raltegravir 1200 mg QD	114/531 (21.5)	170/531 (32.0)	26/531 (4.9)	97/531 (18.3)	63/531 (11.9)	52/531 (9.8)	9/531 (1.7)
	Raltegravir 400 mg BID	57/266 (21.4)	81/266 (30.5)	15/266 (5.6)	50/266 (18.8)	26/266 (9.8)	32/266 (12.0)	5/266 (1.9)
Week 8	Raltegravir 1200 mg QD	215/531 (40.5)	190/531 (35.8)	25/531 (4.7)	46/531 (8.7)	21/531 (4.0)	20/531 (3.8)	14/531 (2.6)
	Raltegravir 400 mg BID	106/266 (39.8)	102/266 (38.3)	11/266 (4.1)	18/266 (6.8)	13/266 (4 9)	8/266 (3.0)	8/266 (3.0)
Week 16	Raltegravir 1200 mg QD	283/531 (53.3)	153/531 (28.8)	19/531 (3.6)	35/531 (6.6)	11/531 (2 1)	7/531 (1.3)	23/531 (4.3)
	Raltegravir 400 mg BID	139/266 (52.3)	83/266 (31.2)	12/266 (4.5)	13/266 (4.9)	7/266 (2.6)	3/266 (1.1)	9/266 (3.4)
Week 24	Raltegravir 1200 mg QD	311/531 (58.6)	153/531 (28.8)	11/531 (2.1)	17/531 (3.2)	8/531 (1 5)	9/531 (1.7)	22/531 (4.1)
	Raltegravir 400 mg BID	152/266 (57.1)	78/266 (29.3)	3/266 (1.1)	13/266 (4.9)	2/266 (0.8)	6/266 (2.3)	12/266 (4.5)
Week 36	Raltegravir 1200 mg QD	333/531 (62.7)	130/531 (24.5)	9/531 (1.7)	10/531 (1.9)	6/531 (1 1)	6/531 (1.1)	37/531 (7.0)
	Raltegravir 400 mg BID	169/266 (63.5)	67/266 (25.2)	6/266 (2.3)	4/266 (1.5)	1/266 (0.4)	2/266 (0.8)	17/266 (6.4)
Week 48	Raltegravir 1200 mg QD	357/531 (67.2)	115/531 (21.7)	5/531 (0.9)	6/531 (1.1)	1/531 (0 2)	6/531 (1.1)	41/531 (7.7)
	Raltegravir 400 mg BID	180/266 (67.7)	55/266 (20.7)	5/266 (1.9)	3/266 (1.1)	0/266 (0.0)	2/266 (0.8)	21/266 (7.9)

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.
N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 19

Change from Baseline in CD4 Cell Count (Cells/mm3) Over Time
Observed Failure Approach

End Point	Visit	Response						Difference in Mean Changes from Baseline [QD - BID]† (95% CI)
		Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
		N	Baseline Mean	Mean Change From Baseline (95% CI)	N	Baseline Mean	Mean Change From Baseline (95% CI)	
Change from baseline in CD4 cell count (cells/mm^3)	Week 24	509	407.9	191.8 (176.8, 206.7)	254	430.4	173 5 (155.0, 192.0)	18.2 (-6.6, 43.0)
	Week 48	499	407.3	232.0 (214.6, 249.4)	251	430.3	234 1 (212.8, 255.3)	-2.1 (-30.9, 26.7)

Approach to handling missing values: Observed Failure (OF) approach assuming baseline-carry-forward for all failures, exclude other missing values. Baseline CD4 Cell Count (Cells/mm^3) was carried forward for subjects who discontinued assigned therapy due to lack of efficacy.

† A positive value means raltegravir 1200 mg QD is better than raltegravir 400 mg BID. The 95% CIs were calculated based on t-distribution.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 20

Log-Rank Test for Time to Virologic Response - by HIV RNA < 40 Copies/mL

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID
	N	Event	Censor	Log-Rank p-Value
Raltegravir 1200 mg QD	531	508	23	0.876
Raltegravir 400 mg BID	266	252	14	

Time to virologic response (TVR) is defined as follows: For subjects who achieved HIV RNA <40 copies/mL, TVR is the time between randomization and the first of two consecutive values (at least 1 week apart) <40 copies/mL; for subjects who did not achieve HIV RNA values <40 copies/mL, TVR is censored at time of the last available visit.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 21

Time to Virologic Response Analysis Using Cox Model - by HIV RNA < 40 Copies/mL

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID		
	N	Event	Censor	Hazard Ratio‡	95% CI for Hazard Ratio	p-Value
Raltegravir 1200 mg QD	531	508	23	1.00	(0.86, 1.16)	0.976
Raltegravir 400 mg BID	266	252	14			

Time to virologic response (TVR) is defined as follows: For subjects who achieved HIV RNA <40 copies/mL, TVR is the time between randomization and the first of two consecutive values (at least 1 week apart) <40 copies/mL; for subjects who did not achieve HIV RNA values <40 copies/mL, TVR is censored at time of the last available visit.

‡ From stratified Cox-model analysis. Screening HIV RNA level (<=100,000 copies/mL or >100,000 copies/mL) is the stratification factor in the model. P-Value is two-sided for testing H0: HR =1 versus H1: HR ≠ 1.

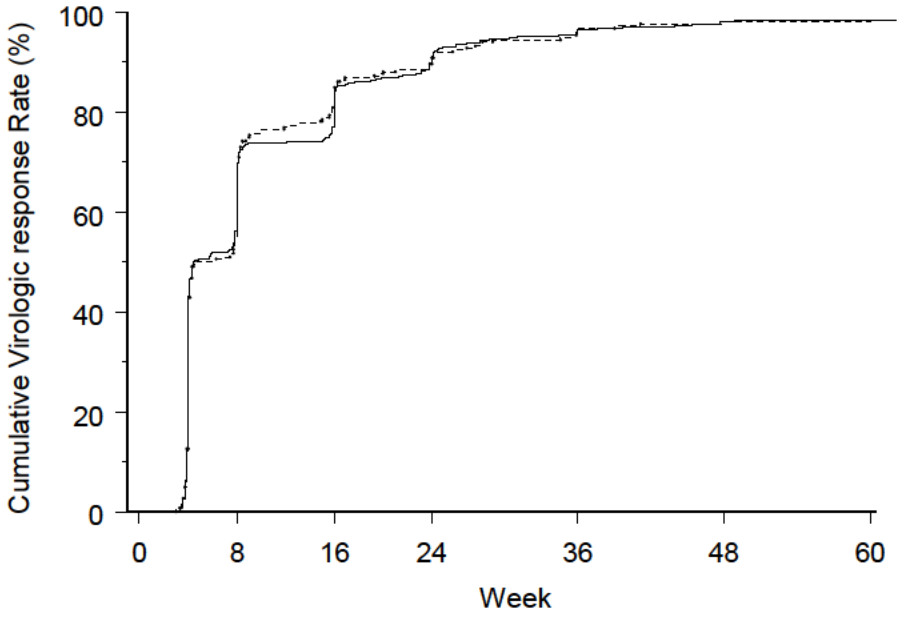
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 4

Kaplan-Meier plot for Time to Virologic Response



Number of Patients at Risk

RAL 1200 mg QD	531	227	117	53	20	7	4
RAL 400 mg BID	266	118	48	26	8	5	1

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 22

Log-Rank Test for Time to Loss of Virologic Response - by HIV RNA ≥ 40 Copies/mL

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID
	N	Event	Censor	Log-Rank p-Value
Raltegravir 1200 mg QD	531	63	468	0.836
Raltegravir 400 mg BID	266	33	233	

Time to loss of virologic response (TLOVR) is defined as follows: For subjects who had confirmed HIV RNA levels below an assay limit (40 copies/mL) (on two consecutive visits), TLOVR is the time between randomization and the first of two consecutive values (at least 1 week apart) above the assay limit of 40 copies/mL or loss to follow-up after achieving confirmed HIV-1 RNA <40 copies/mL; For subjects who achieve and sustain HIV-1 RNA <40 copies/mL, TLOVR is censored at the time of last available visit; For subjects who never achieved confirmed HIV RNA levels below the assay limit (on two consecutive visits), TLOVR is time 0.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 23

Time to Loss of Virologic Response Analysis Using Cox Model - by HIV RNA ≥ 40 Copies/mL

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID		
	N	Event	Censor	Hazard Ratio‡	95% CI for Hazard Ratio	p-Value
Raltegravir 1200 mg QD	531	63	468	0.95	(0.63, 1.45)	0.823
Raltegravir 400 mg BID	266	33	233			

Time to loss of virologic response (TLOVR) is defined as follows: For subjects who had confirmed HIV RNA levels below an assay limit (40 copies/mL) (on two consecutive visits), TLOVR is the time between randomization and the first of two consecutive values (at least 1 week apart) above the assay limit of 40 copies/mL or loss to follow-up after achieving confirmed HIV-1 RNA <40 copies/mL; For subjects who achieve and sustain HIV-1 RNA <40 copies/mL, TLOVR is censored at the time of last available visit; For subjects who never achieved confirmed HIV RNA levels below the assay limit (on two consecutive visits), TLOVR is time 0.

‡ From stratified Cox-model analysis. Screening HIV RNA level (<=100,000 copies/mL or >100,000 copies/mL) is the stratification factor in the model. P-Value is two-sided for testing H0: HR =1 versus H1: HR ≠ 1.

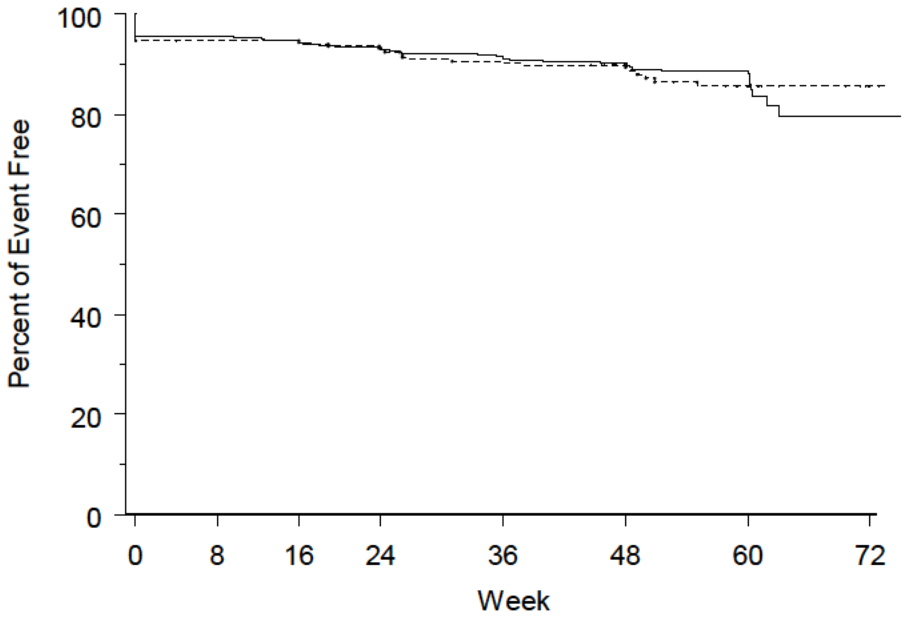
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 5

Kaplan-Meier plot for Time to Loss of Virologic Response



Number of Patients at Risk

——— RAL 1200 mg QD	531	508	503	495	485	414	168	25
- - - - - - - RAL 400 mg BID	266	252	252	248	241	210	73	11

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 24

Log-Rank Test for Time to Loss of Virologic Response - by HIV RNA ≥ 40 Copies/mL Supportive

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID
	N	Event	Censor	Log-Rank p-Value
Raltegravir 1200 mg QD	531	77	454	0.780
Raltegravir 400 mg BID	266	41	225	

Time to loss of virologic response (TLOVR) is defined as follows: For subjects who had confirmed HIV RNA levels below an assay limit (40 copies/mL) (on two consecutive visits) by Week 24, TLOVR is the time between randomization and the first of two consecutive values (at least 1 week apart) above the assay limit of 40 copies/mL or loss to follow-up after achieving confirmed HIV-1 RNA <40 copies/mL; For subjects who achieve and sustain HIV-1 RNA <40 copies/mL, TLOVR is censored at the time of last available visit; For subjects who never achieved confirmed HIV RNA levels below the assay limit (on two consecutive visits) by Week 24, TLOVR is 24 weeks.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 25

Time to Loss of Virologic Response Analysis Using Cox Model - by HIV RNA ≥ 40 Copies/mL Supportive

Treatment	Summary of Log-Rank			Raltegravir 1200 mg QD Compared with Raltegravir 400 mg BID		
	N	Event	Censor	Hazard Ratio‡	95% CI for Hazard Ratio	p-Value
Raltegravir 1200 mg QD	531	77	454	0.94	(0.64, 1.37)	0.752
Raltegravir 400 mg BID	266	41	225			

Time to loss of virologic response (TLOVR) is defined as follows: For subjects who had confirmed HIV RNA levels below an assay limit (40 copies/mL) (on two consecutive visits) by Week 24, TLOVR is the time between randomization and the first of two consecutive values (at least 1 week apart) above the assay limit of 40 copies/mL or loss to follow-up after achieving confirmed HIV-1 RNA <40 copies/mL; For subjects who achieve and sustain HIV-1 RNA <40 copies/mL, TLOVR is censored at the time of last available visit; For subjects who never achieved confirmed HIV RNA levels below the assay limit (on two consecutive visits) by Week 24, TLOVR is 24 weeks.

‡ From stratified Cox-model analysis. Screening HIV RNA level (<=100,000 copies/mL or >100,000 copies/mL) is the stratification factor in the model. P-Value is two-sided for testing H0: HR =1 versus H1: HR ≠ 1.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 26

Proportion of Subjects with Plasma HIV RNA <40 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	472/501	94.2 (91.8, 96.1)	235/251	93.6 (89.9, 96.3)	0.6 (-2.8, 4.7)
Baseline Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	348/358	97.2 (94.9, 98.7)	173/177	97.7 (94.3, 99.4)	-0.5 (-3.2, 3.1)
>100,000 copies/mL	124/143	86.7 (80.0, 91.8)	62/74	83.8 (73.4, 91.3)	2.9 (-6.5, 14.1)
Baseline Plasma HIV RNA (copies/mL)					
≤500,000 copies/mL	456/479	95.2 (92.9, 96.9)	227/237	95.8 (92.4, 98.0)	-0.6 (-3.6, 3.1)
>500,000 copies/mL	16/22	72.7 (49.8, 89.3)	8/14	57.1 (28.9, 82.3)	15.6 (-15.6, 45.9)
Screening Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	345/357	96.6 (94.2, 98.3)	173/178	97.2 (93.6, 99.1)	-0.6 (-3.5, 3.3)
>100,000 copies/mL	127/144	88.2 (81.8, 93.0)	62/73	84.9 (74.6, 92.2)	3.3 (-5.8, 14.2)
Baseline CD4 Cell Counts (cells/mm^3)					
≤50 cells/mm^3	6/9	66.7 (29.9, 92.5)	4/5	80.0 (28.4, 99.5)	-13.3 (-53.7, 38.9)
>50 cells/mm^3 and ≤200 cells/mm^3	51/58	87.9 (76.7, 95.0)	25/28	89.3 (71.8, 97.7)	-1.4 (-14.7, 16.5)
>200 cells/mm^3	415/434	95.6 (93.2, 97.3)	206/218	94.5 (90.6, 97.1)	1.1 (-2.2, 5.3)
Hepatitis Status[‡]					
Hepatitis B and/or C Positive	13/13	100.0 (75.3, 100.0)	6/7	85.7 (42.1, 99.6)	14.3 (-11.7, 52.2)
Both Hepatitis B and C Negative	459/488	94.1 (91.6, 96.0)	229/244	93.9 (90.1, 96.5)	0.2 (-3.3, 4.3)
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use					
Yes	51/57	89.5 (78.5, 96.0)	37/39	94.9 (82.7, 99.4)	-5.4 (-17.0, 7.6)
No	421/444	94.8 (92.3, 96.7)	198/212	93.4 (89.2, 96.3)	1.4 (-2.2, 5.9)
Age (years)					
18 to 64	469/497	94.4 (92.0, 96.2)	232/248	93.5 (89.7, 96.3)	0.8 (-2.6, 5.0)
≥65	3/4	75.0 (19.4, 99.4)	3/3	100.0 (29.2, 100.0)	-25.0 (-72.3, 43.8)
Age (years)					
≤Median	242/257	94.2 (90.6, 96.7)	108/117	92.3 (85.9, 96.4)	1.9 (-3.2, 8.6)
>Median	230/244	94.3 (90.6, 96.8)	127/134	94.8 (89.5, 97.9)	-0.5 (-5.1, 5.1)

Proportion of Subjects with Plasma HIV RNA <40 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Gender					
Male	393/415	94.7 (92.1, 96.6)	206/220	93.6 (89.6, 96.5)	1.1 (-2.6, 5.5)
Female	79/86	91.9 (83.9, 96.7)	29/31	93.5 (78.6, 99.2)	-1.7 (-11.1, 13.3)
Race					
American Indian or Alaska Native	3/3	100.0 (29.2, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-60.6, 60.6)
Asian	76/81	93.8 (86.2, 98.0)	36/39	92.3 (79.1, 98.4)	1.5 (-7.7, 14.8)
Black or African American	83/93	89.2 (81.1, 94.7)	29/33	87.9 (71.8, 96.6)	1.4 (-9.7, 17.5)
Multiple	40/43	93.0 (80.9, 98.5)	13/14	92.9 (66.1, 99.8)	0.2 (-13.5, 25.4)
Native Hawaiian or Other Pacific Islander	0/0	N/A	1/1	100.0 (2.5, 100.0)	N/A
White	270/281	96.1 (93.1, 98.0)	153/161	95.0 (90.4, 97.8)	1.1 (-2.8, 5.9)
Ethnicity					
Hispanic or Latino	113/118	95.8 (90.4, 98.6)	48/49	98.0 (89.1, 99.9)	-2.2 (-7.9, 6.8)
Not Hispanic or Latino	336/358	93.9 (90.8, 96.1)	178/193	92.2 (87.5, 95.6)	1.6 (-2.6, 6.7)
Not Reported	17/19	89.5 (66.9, 98.7)	8/8	100.0 (63.1, 100.0)	-10.5 (-31.9, 24.0)
Unknown	6/6	100.0 (54.1, 100.0)	1/1	100.0 (2.5, 100.0)	0.0 (-42.8, 81.8)
Region					
Africa	39/41	95.1 (83.5, 99.4)	12/12	100.0 (73.5, 100.0)	-4.9 (-16.3, 20.0)
Asia/Pacific	79/84	94.0 (86.7, 98.0)	40/43	93.0 (80.9, 98.5)	1.0 (-7.7, 13.3)
Europe	183/190	96.3 (92.6, 98.5)	102/108	94.4 (88.3, 97.9)	1.9 (-2.9, 8.2)
Latin America	69/73	94.5 (86.6, 98.5)	26/26	100.0 (86.8, 100.0)	-5.5 (-13.3, 7.7)
North America	102/113	90.3 (83.2, 95.0)	55/62	88.7 (78.1, 95.3)	1.6 (-7.5, 12.7)
Viral Subtype					
Clade B	296/313	94.6 (91.4, 96.8)	164/175	93.7 (89.0, 96.8)	0.9 (-3.3, 5.9)
Non-Clade B	175/187	93.6 (89.1, 96.6)	69/74	93.2 (84.9, 97.8)	0.3 (-5.7, 8.9)
Missing	1/1	100.0 (2.5, 100.0)	2/2	100.0 (15.8, 100.0)	0.0 (-85.2, 74.2)

[†] The 95% CIs were calculated using Miettinen and Nurminen's method.

[‡] Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.

[§] Subjects who took at least one dose of PPI/H2 blocker during treatment period.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

n = Number of subjects in each subcategory.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 27

Proportion of Subjects with Plasma HIV RNA <50 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	477/501	95.2 (93.0, 96.9)	240/251	95.6 (92.3, 97.8)	-0.4 (-3.4, 3.2)
Baseline Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	350/358	97.8 (95.6, 99.0)	175/177	98.9 (96.0, 99.9)	-1.1 (-3.4, 1.9)
>100,000 copies/mL	127/143	88.8 (82.5, 93.5)	65/74	87.8 (78.2, 94.3)	1.0 (-7.5, 11.3)
Baseline Plasma HIV RNA (copies/mL)					
≤500,000 copies/mL	460/479	96.0 (93.9, 97.6)	230/237	97.0 (94.0, 98.8)	-1.0 (-3.7, 2.3)
>500,000 copies/mL	17/22	77.3 (54.6, 92.2)	10/14	71.4 (41.9, 91.6)	5.8 (-22.3, 36.4)
Screening Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	346/357	96.9 (94.6, 98.5)	175/178	98.3 (95.2, 99.7)	-1.4 (-4.1, 2.0)
>100,000 copies/mL	131/144	91.0 (85.1, 95.1)	65/73	89.0 (79.5, 95.1)	1.9 (-6.0, 11.9)
Baseline CD4 Cell Counts (cells/mm^3)					
≤50 cells/mm^3	6/9	66.7 (29.9, 92.5)	4/5	80.0 (28.4, 99.5)	-13.3 (-53.7, 38.9)
>50 cells/mm^3 and ≤200 cells/mm^3	52/58	89.7 (78.8, 96.1)	26/28	92.9 (76.5, 99.1)	-3.2 (-15.4, 13.4)
>200 cells/mm^3	419/434	96.5 (94.4, 98.1)	210/218	96.3 (92.9, 98.4)	0.2 (-2.6, 3.9)
Hepatitis Status[‡]					
Hepatitis B and/or C Positive	13/13	100.0 (75.3, 100.0)	6/7	85.7 (42.1, 99.6)	14.3 (-11.7, 52.2)
Both Hepatitis B and C Negative	464/488	95.1 (92.8, 96.8)	234/244	95.9 (92.6, 98.0)	-0.8 (-3.8, 2.8)
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use					
Yes	52/57	91.2 (80.7, 97.1)	37/39	94.9 (82.7, 99.4)	-3.6 (-14.8, 9.2)
No	425/444	95.7 (93.4, 97.4)	203/212	95.8 (92.1, 98.0)	-0.0 (-3.1, 3.9)
Age (years)					
18 to 64	473/497	95.2 (92.9, 96.9)	237/248	95.6 (92.2, 97.8)	-0.4 (-3.4, 3.3)
≥65	4/4	100.0 (39.8, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-52.8, 59.9)
Age (years)					
≤Median	245/257	95.3 (92.0, 97.6)	111/117	94.9 (89.2, 98.1)	0.5 (-3.9, 6.4)
>Median	232/244	95.1 (91.6, 97.4)	129/134	96.3 (91.5, 98.8)	-1.2 (-5.3, 3.9)

Proportion of Subjects with Plasma HIV RNA <50 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Gender					
Male	398/415	95.9 (93.5, 97.6)	210/220	95.5 (91.8, 97.8)	0.4 (-2.7, 4.4)
Female	79/86	91.9 (83.9, 96.7)	30/31	96.8 (83.3, 99.9)	-4.9 (-13.5, 8.7)
Race					
American Indian or Alaska Native	3/3	100.0 (29.2, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-60.6, 60.6)
Asian	77/81	95.1 (87.8, 98.6)	37/39	94.9 (82.7, 99.4)	0.2 (-8.0, 12.4)
Black or African American	84/93	90.3 (82.4, 95.5)	30/33	90.9 (75.7, 98.1)	-0.6 (-10.6, 14.7)
Multiple	41/43	95.3 (84.2, 99.4)	13/14	92.9 (66.1, 99.8)	2.5 (-10.2, 27.5)
Native Hawaiian or Other Pacific Islander	0/0	N/A	1/1	100.0 (2.5, 100.0)	N/A
White	272/281	96.8 (94.0, 98.5)	156/161	96.9 (92.9, 99.0)	-0.1 (-3.4, 4.1)
Ethnicity					
Hispanic or Latino	114/118	96.6 (91.5, 99.1)	48/49	98.0 (89.1, 99.9)	-1.3 (-6.8, 7.6)
Not Hispanic or Latino	340/358	95.0 (92.2, 97.0)	183/193	94.8 (90.7, 97.5)	0.2 (-3.5, 4.6)
Not Reported	17/19	89.5 (66.9, 98.7)	8/8	100.0 (63.1, 100.0)	-10.5 (-31.9, 24.0)
Unknown	6/6	100.0 (54.1, 100.0)	1/1	100.0 (2.5, 100.0)	0.0 (-42.8, 81.8)
Region					
Africa	39/41	95.1 (83.5, 99.4)	12/12	100.0 (73.5, 100.0)	-4.9 (-16.3, 20.0)
Asia/Pacific	80/84	95.2 (88.3, 98.7)	41/43	95.3 (84.2, 99.4)	-0.1 (-7.9, 11.2)
Europe	185/190	97.4 (94.0, 99.1)	103/108	95.4 (89.5, 98.5)	2.0 (-2.3, 8.0)
Latin America	70/73	95.9 (88.5, 99.1)	26/26	100.0 (86.8, 100.0)	-4.1 (-11.5, 9.0)
North America	103/113	91.2 (84.3, 95.7)	58/62	93.5 (84.3, 98.2)	-2.4 (-10.4, 7.4)
Viral Subtype					
Clade B	299/313	95.5 (92.6, 97.5)	168/175	96.0 (91.9, 98.4)	-0.5 (-4.1, 3.9)
Non-Clade B	177/187	94.7 (90.4, 97.4)	70/74	94.6 (86.7, 98.5)	0.1 (-5.4, 8.1)
Missing	1/1	100.0 (2.5, 100.0)	2/2	100.0 (15.8, 100.0)	0.0 (-85.2, 74.2)

[†] The 95% CIs were calculated using Miettinen and Nurminen's method.

[‡] Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.

[§] Subjects who took at least one dose of PPI/H2 blocker during treatment period.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

n = Number of subjects in each subcategory.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 28

Proportion of Subjects with Plasma HIV RNA <200 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	484/501	96.6 (94.6, 98.0)	243/251	96.8 (93.8, 98.6)	-0.2 (-2.8, 3.0)
Baseline Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	351/358	98.0 (96.0, 99.2)	175/177	98.9 (96.0, 99.9)	-0.8 (-3.1, 2.2)
>100,000 copies/mL	133/143	93.0 (87.5, 96.6)	68/74	91.9 (83.2, 97.0)	1.1 (-5.9, 10.2)
Baseline Plasma HIV RNA (copies/mL)					
≤500,000 copies/mL	465/479	97.1 (95.1, 98.4)	232/237	97.9 (95.1, 99.3)	-0.8 (-3.1, 2.1)
>500,000 copies/mL	19/22	86.4 (65.1, 97.1)	11/14	78.6 (49.2, 95.3)	7.8 (-17.4, 36.8)
Screening Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	349/357	97.8 (95.6, 99.0)	175/178	98.3 (95.2, 99.7)	-0.6 (-3.0, 2.8)
>100,000 copies/mL	135/144	93.8 (88.5, 97.1)	68/73	93.2 (84.7, 97.7)	0.6 (-6.0, 9.4)
Baseline CD4 Cell Counts (cells/mm^3)					
≤50 cells/mm^3	6/9	66.7 (29.9, 92.5)	4/5	80.0 (28.4, 99.5)	-13.3 (-53.7, 38.9)
>50 cells/mm^3 and ≤200 cells/mm^3	52/58	89.7 (78.8, 96.1)	26/28	92.9 (76.5, 99.1)	-3.2 (-15.4, 13.4)
>200 cells/mm^3	426/434	98.2 (96.4, 99.2)	213/218	97.7 (94.7, 99.3)	0.5 (-1.7, 3.6)
Hepatitis Status[‡]					
Hepatitis B and/or C Positive	13/13	100.0 (75.3, 100.0)	6/7	85.7 (42.1, 99.6)	14.3 (-11.7, 52.2)
Both Hepatitis B and C Negative	471/488	96.5 (94.5, 98.0)	237/244	97.1 (94.2, 98.8)	-0.6 (-3.2, 2.6)
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use					
Yes	55/57	96.5 (87.9, 99.6)	37/39	94.9 (82.7, 99.4)	1.6 (-7.7, 13.9)
No	429/444	96.6 (94.5, 98.1)	206/212	97.2 (93.9, 99.0)	-0.5 (-3.2, 2.9)
Age (years)					
18 to 64	480/497	96.6 (94.6, 98.0)	240/248	96.8 (93.7, 98.6)	-0.2 (-2.8, 3.1)
≥65	4/4	100.0 (39.8, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-52.8, 59.9)
Age (years)					
≤Median	250/257	97.3 (94.5, 98.9)	113/117	96.6 (91.5, 99.1)	0.7 (-2.8, 5.9)
>Median	234/244	95.9 (92.6, 98.0)	130/134	97.0 (92.5, 99.2)	-1.1 (-4.9, 3.7)

Proportion of Subjects with Plasma HIV RNA <200 Copies/mL at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Gender					
Male	403/415	97.1 (95.0, 98.5)	213/220	96.8 (93.6, 98.7)	0.3 (-2.4, 3.8)
Female	81/86	94.2 (87.0, 98.1)	30/31	96.8 (83.3, 99.9)	-2.6 (-10.5, 10.8)
Race					
American Indian or Alaska Native	3/3	100.0 (29.2, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-60.6, 60.6)
Asian	79/81	97.5 (91.4, 99.7)	38/39	97.4 (86.5, 99.9)	0.1 (-6.5, 11.0)
Black or African American	84/93	90.3 (82.4, 95.5)	30/33	90.9 (75.7, 98.1)	-0.6 (-10.6, 14.7)
Multiple	41/43	95.3 (84.2, 99.4)	14/14	100.0 (76.8, 100.0)	-4.7 (-15.6, 17.5)
Native Hawaiian or Other Pacific Islander	0/0	N/A	1/1	100.0 (2.5, 100.0)	N/A
White	277/281	98.6 (96.4, 99.6)	157/161	97.5 (93.8, 99.3)	1.1 (-1.6, 4.9)
Ethnicity					
Hispanic or Latino	116/118	98.3 (94.0, 99.8)	49/49	100.0 (92.7, 100.0)	-1.7 (-6.0, 5.7)
Not Hispanic or Latino	344/358	96.1 (93.5, 97.8)	185/193	95.9 (92.0, 98.2)	0.2 (-3.1, 4.4)
Not Reported	18/19	94.7 (74.0, 99.9)	8/8	100.0 (63.1, 100.0)	-5.3 (-25.1, 28.7)
Unknown	6/6	100.0 (54.1, 100.0)	1/1	100.0 (2.5, 100.0)	0.0 (-42.8, 81.8)
Region					
Africa	39/41	95.1 (83.5, 99.4)	12/12	100.0 (73.5, 100.0)	-4.9 (-16.3, 20.0)
Asia/Pacific	82/84	97.6 (91.7, 99.7)	42/43	97.7 (87.7, 99.9)	-0.1 (-6.4, 9.9)
Europe	188/190	98.9 (96.2, 99.9)	104/108	96.3 (90.8, 99.0)	2.7 (-0.7, 8.2)
Latin America	71/73	97.3 (90.5, 99.7)	26/26	100.0 (86.8, 100.0)	-2.7 (-9.5, 10.3)
North America	104/113	92.0 (85.4, 96.3)	59/62	95.2 (86.5, 99.0)	-3.1 (-10.6, 6.1)
Viral Subtype					
Clade B	302/313	96.5 (93.8, 98.2)	169/175	96.6 (92.7, 98.7)	-0.1 (-3.4, 4.1)
Non-Clade B	181/187	96.8 (93.1, 98.8)	72/74	97.3 (90.6, 99.7)	-0.5 (-4.7, 6.3)
Missing	1/1	100.0 (2.5, 100.0)	2/2	100.0 (15.8, 100.0)	0.0 (-85.2, 74.2)

[†] The 95% CIs were calculated using Miettinen and Nurminen's method.

[‡] Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.

[§] Subjects who took at least one dose of PPI/H2 blocker during treatment period.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

n = Number of subjects in each subcategory.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 29

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48
by Prognostic and Demographic Factors
Observed Failure Approach

Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID]† (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Total	499	407.3	232.0 (214.6, 249.4)	251	430.3	234.1 (212.8, 255.3)	-2.1 (-30.9, 26.7)
Baseline Plasma HIV RNA (copies/mL)							
≤100,000 copies/mL	358	431.0	214.4 (193.8, 235.1)	177	471.3	224.9 (199.2, 250.5)	-10.4 (-44.8, 24.0)
>100,000 copies/mL	141	347.2	276.4 (245.0, 307.9)	74	332.3	256.0 (217.8, 294.3)	20.4 (-30.9, 71.7)
Baseline Plasma HIV RNA (copies/mL)							
≤500,000 copies/mL	477	413.1	228.0 (210.7, 245.3)	237	444.2	237.4 (215.4, 259.5)	-9.5 (-38.5, 19.5)
>500,000 copies/mL	22	281.7	318.9 (191.3, 446.5)	14	194.9	176.7 (96.9, 256.5)	142.2 (-25.7, 310.1)
Screening Plasma HIV RNA (copies/mL)							
≤100,000 copies/mL	358	434.5	215.8 (195.0, 236.6)	177	475.6	226.4 (200.5, 252.4)	-10.6 (-45.3, 24.1)
>100,000 copies/mL	141	338.3	273.1 (242.0, 304.2)	74	322.1	252.3 (215.0, 289.6)	20.7 (-29.7, 71.2)
Baseline CD4 Cell Counts (cells/mm^3)							
≤50 cells/mm^3	9	22.7	185.4 (45.2, 325.7)	5	19.8	212.8 (33.4, 392.2)	-27.4 (-234.9, 180.2)
>50 cells/mm^3 and ≤200 cells/mm^3	57	145.1	212.9 (178.6, 247.2)	27	138.0	207.7 (169.8, 245.7)	5.2 (-50.4, 60.8)
>200 cells/mm^3	433	449.8	235.4 (216.0, 254.9)	219	475.7	237.8 (214.0, 261.6)	-2.3 (-34.4, 29.7)
Hepatitis Status‡							
Hepatitis B and/or C Positive	13	392.0	121.2 (31.9, 210.5)	7	422.1	145.9 (67.7, 224.0)	-24.7 (-152.9, 103.5)
Both Hepatitis B and C Negative	486	407.7	234.9 (217.2, 252.6)	244	430.6	236.6 (214.9, 258.3)	-1.7 (-30.9, 27.6)

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID][†] (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use							
Yes	58	408.4	228.0 (159.4, 296.6)	39	445.3	225.3 (163.8, 286.8)	2.7 (-93.9, 99.3)
No	441	407.2	232.5 (214.8, 250.1)	212	427.6	235.7 (212.9, 258.4)	-3.2 (-33.1, 26.7)
Age (years)							
18 to 64	495	404.9	234.1 (217.5, 250.7)	248	429.3	235.0 (213.6, 256.5)	-0.9 (-28.8, 27.0)
≥65	4	698.0	-34.3 (-1252.4, 1183.9)	3	513.0	154.7 (-141.1, 450.5)	-188.9 (-1362.5, 984.6)
Age (years)							
≤Median	257	405.4	238.7 (216.7, 260.7)	118	424.9	231.4 (201.5, 261.2)	7.3 (-30.8, 45.5)
>Median	242	409.3	224.8 (197.4, 252.2)	133	435.2	236.4 (205.9, 266.9)	-11.6 (-54.8, 31.5)
Gender							
Male	414	426.5	235.3 (215.5, 255.1)	220	445.7	235.5 (212.3, 258.7)	-0.2 (-32.1, 31.8)
Female	85	313.7	215.6 (181.1, 250.1)	31	321.2	223.9 (170.8, 277.0)	-8.3 (-73.2, 56.6)
Race							
American Indian or Alaska Native	3	473.7	237.7 (-698.4, 1173.7)	3	452.0	225.7 (-52.4, 503.8)	12.0 (-618.1, 642.1)
Asian	81	371.2	259.6 (224.3, 294.9)	39	362.5	220.8 (172.5, 269.1)	38.8 (-21.5, 99.1)
Black or African American	93	351.4	212.9 (162.6, 263.2)	33	360.6	230.1 (173.6, 286.6)	-17.2 (-107.7, 73.3)
Multiple	42	376.2	239.6 (191.7, 287.5)	13	384.9	303.1 (223.6, 382.5)	-63.5 (-158.3, 31.4)
Native Hawaiian or Other Pacific Islander	0	N/A	N/A	1	334.0	72.0 (N/A)	N/A
White	280	440.3	229.1 (206.1, 252.0)	162	464.7	233.7 (205.4, 261.9)	-4.6 (-41.5, 32.4)

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48 by Prognostic and Demographic Factors Observed Failure Approach

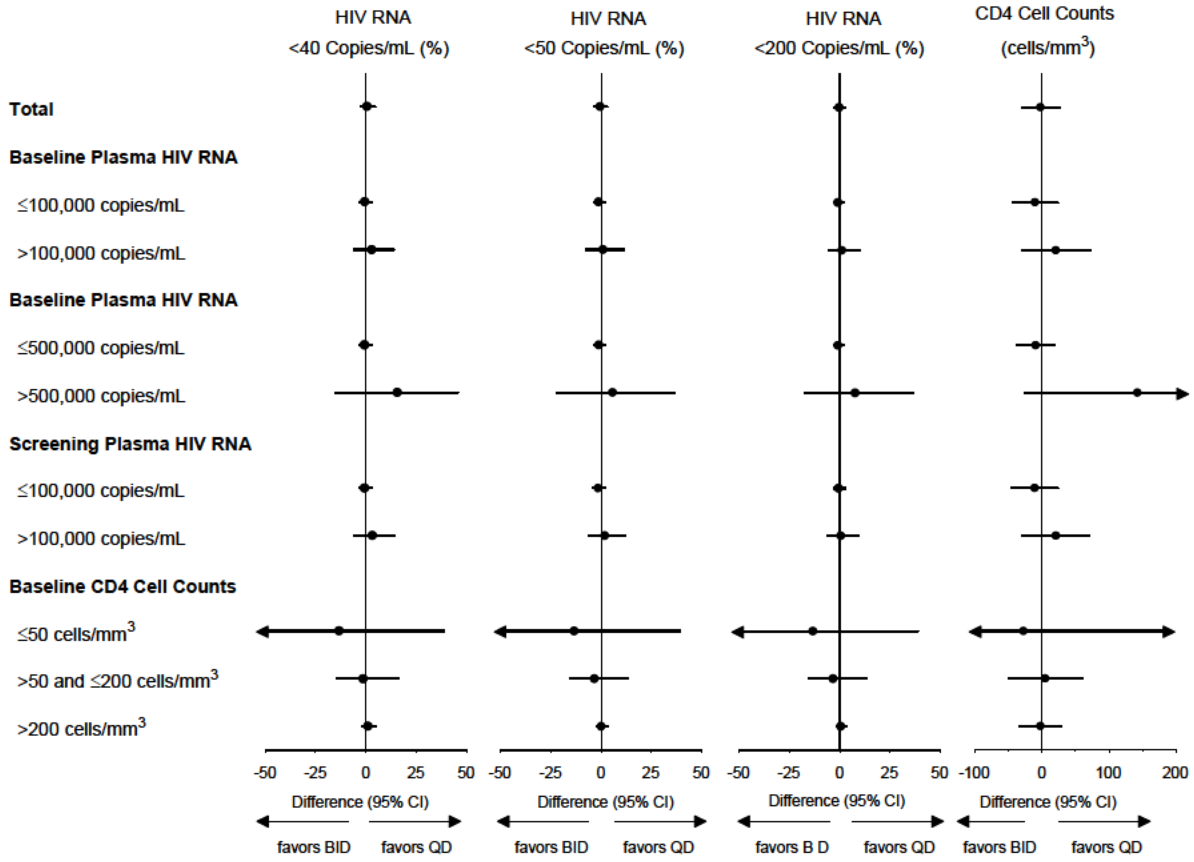
Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID]† (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Ethnicity							
Hispanic or Latino	119	427.3	248.7 (214.6, 282.7)	48	460.0	241.8 (188.6, 295.1)	6.8 (-56.1, 69.8)
Not Hispanic or Latino	355	400.5	219.7 (199.0, 240.3)	194	422.1	232.5 (208.4, 256.5)	-12.8 (-45.8, 20.3)
Not Reported	19	379.7	296.2 (207.0, 385.3)	8	485.3	244.4 (128.8, 360.0)	51.8 (-98.6, 202.1)
Unknown	6	498.0	423.5 (92.8, 754.2)	1	157.0	83.0 (N/A)	340.5 (-534.4, 1215.4)
Region							
Africa	41	272.4	216.0 (164.3, 267.7)	12	264.6	236.1 (158.3, 313.8)	-20.1 (-122.7, 82.5)
Asia/Pacific	84	354.8	250.4 (213.8, 287.0)	43	366.9	219.3 (175.3, 263.2)	31.1 (-28.4, 90.7)
Europe	189	447.6	229.1 (199.8, 258.4)	108	464.8	226.3 (192.8, 259.7)	2.9 (-43.2, 49.0)
Latin America	73	412.8	241.7 (202.5, 280.9)	26	403.3	281.8 (209.1, 354.4)	-40.1 (-117.7, 37.5)
North America	112	424.5	222.4 (178.4, 266.5)	62	457.7	237.5 (190.1, 284.9)	-15.1 (-83.6, 53.5)
Viral Subtype							
Clade B	311	423.6	231.6 (209.1, 254.1)	175	461.9	239.7 (213.3, 266.1)	-8.1 (-44.0, 27.7)
Non-Clade B	187	380.0	232.8 (205.0, 260.7)	74	349.8	225.8 (190.8, 260.8)	7.0 (-42.3, 56.3)
Missing	1	426.0	187.0 (N/A)	2	650.0	43.5 (-2898.0, 2985.0)	143.5 (-4951.3, 5238.3)

† The 95% CIs were based on t-distribution.
‡ Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.
§ Subjects who took at least one dose of PPI/H2 blocker during treatment period.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.
N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 6

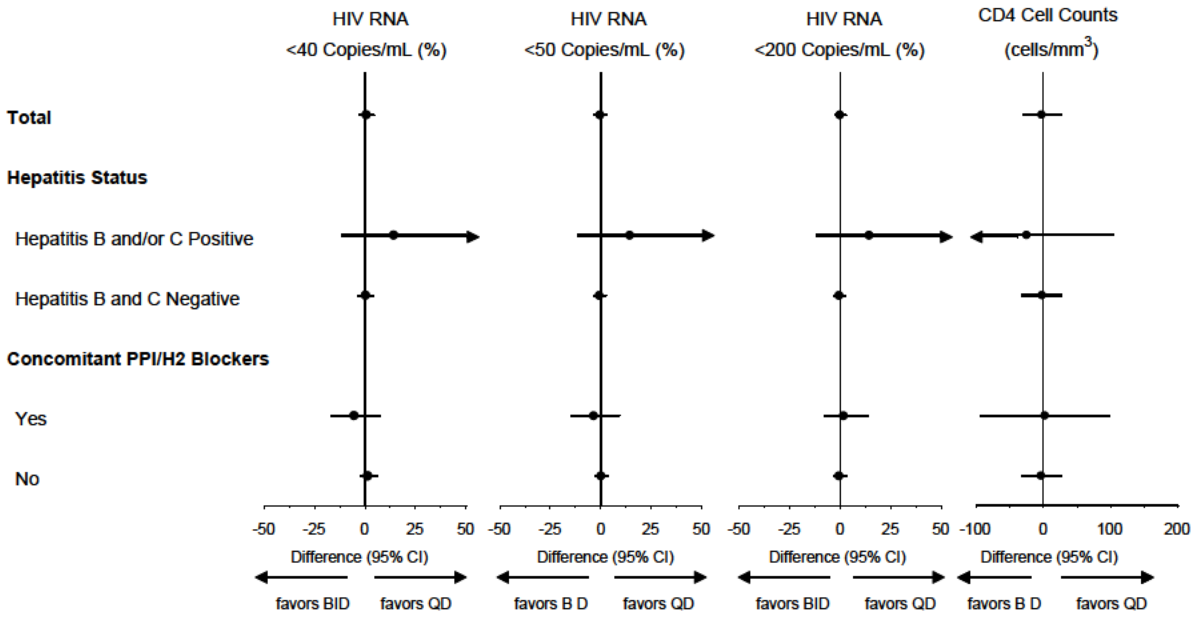
Efficacy Analysis at Week 48 by Baseline and Screening HIV RNA (copies/mL) and Baseline CD4 Cell Count (cells/mm^3) Categories
Difference Between Treatment Groups (QD-BID)
Observed Failure Approach



Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 7

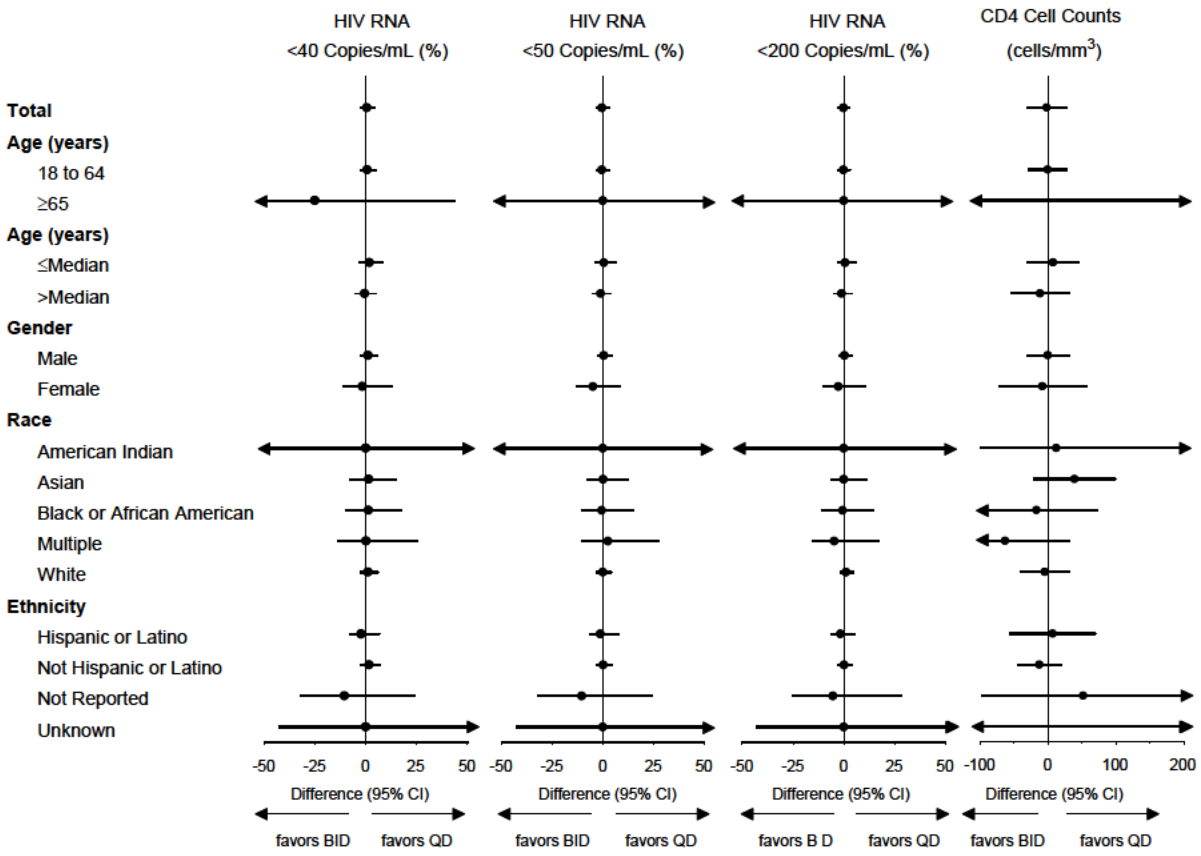
Efficacy Analysis at Week 48 by Hepatitis Status and Proton Pump Inhibitor/H_2 Blocker Use
Difference Between Treatment Groups (QD-BID)
Observed Failure Approach



Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 8

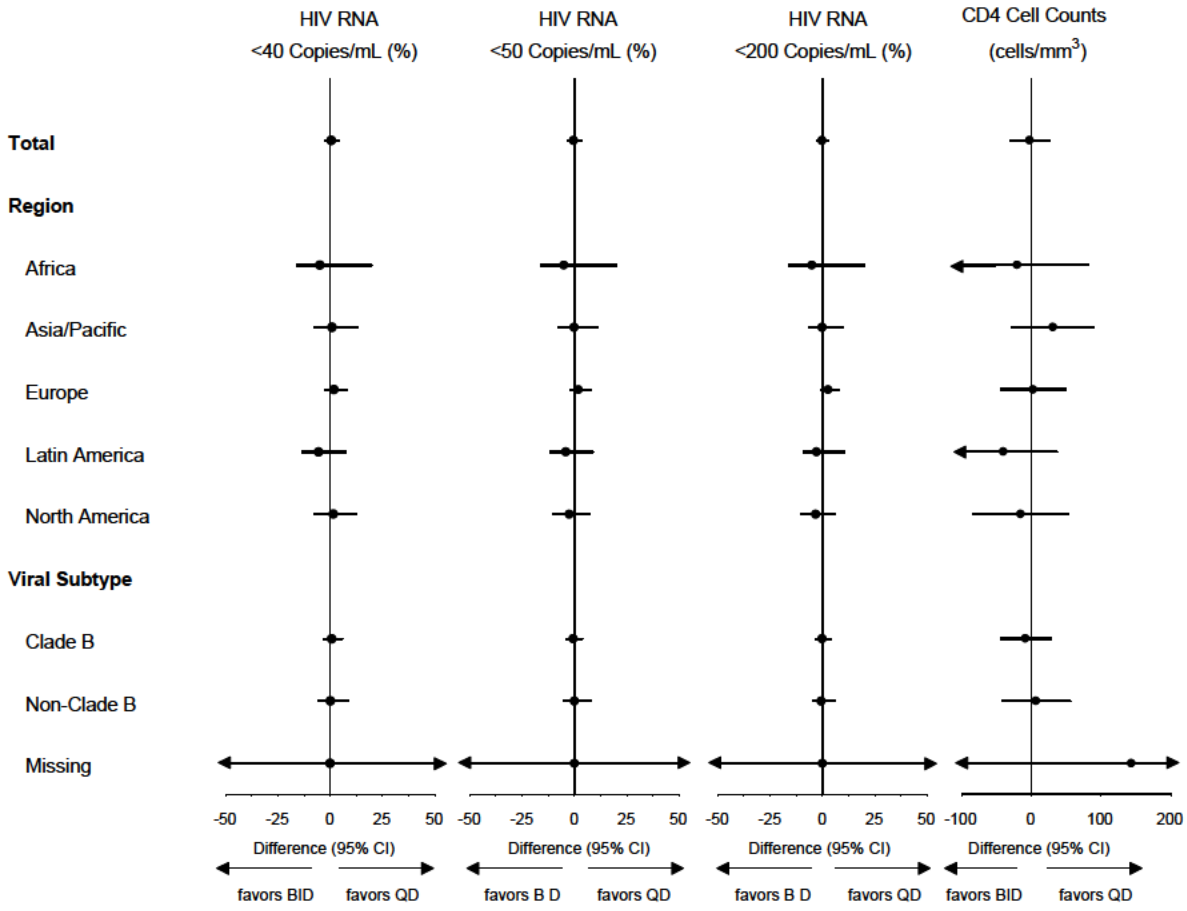
Efficacy Analysis at Week 48 by Age, Gender, Race, and Ethnicity
Difference Between Treatment Groups (QD-BID)
Observed Failure Approach



Data Source: [Ref. 5.3.5.1: P292V01]

Figure 2.7.3-qd1200: 9

Efficacy Analysis at Week 48 by Region and Viral Subtype
Difference Between Treatment Groups (QD-BID)
Observed Failure Approach



Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 30

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3005*			Baseline	1	107545	Rebounder	Week 48 (340)	Y
				Week 4	28	115	Rebounder	Week 48 (340)	Y
				Week 8	56	58	Rebounder	Week 48 (340)	Y
				Week 16	108	<40 TND	Rebounder	Week 48 (340)	Y
				Week 24	165	<40 TD	Rebounder	Week 48 (340)	Y
				Week 36	252	55	Rebounder	Week 48 (340)	Y
				Week 36	263	<40 TND	Rebounder	Week 48 (340)	Y
				Week 48	340	63	Rebounder	Week 48 (340)	Y
				Week 48	350	64	Rebounder	Week 48 (340)	Y
				Week 48	364	<40 TD	Rebounder	Week 48 (340)	Y
				Week 60	424	<40 TND	Rebounder	Week 48 (340)	Y
				Week 72	512	<40 TD	Rebounder	Week 48 (340)	Y
	P3008*			Baseline	1	523	Rebounder	Week 16 (113)	Y
				Week 4	29	<40 TD	Rebounder	Week 16 (113)	Y
				Week 8	57	<40 TND	Rebounder	Week 16 (113)	Y
				Week 16	113	137	Rebounder	Week 16 (113)	Y
				Week 24	141	40	Rebounder	Week 16 (113)	Y
				Week 24	169	<40 TD	Rebounder	Week 16 (113)	Y
				Week 36	253	<40 TD	Rebounder	Week 16 (113)	Y
				Week 48	337	<40 TND	Rebounder	Week 16 (113)	Y
				Week 60	421	<40 TND	Rebounder	Week 16 (113)	Y
				Week 72	505	<40 TND	Rebounder	Week 16 (113)	Y

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3009*	DISCONTINUED (LOST TO FOLLOW-UP)	153	Baseline	1	8273	Rebounder	Week 16 (114)	
				Week 4	31	<40 TND	Rebounder	Week 16 (114)	
				Week 8	59	<40 TND	Rebounder	Week 16 (114)	
				Week 16	114	10899	Rebounder	Week 16 (114)	
				Week 16	135	509	Rebounder	Week 16 (114)	
	P3010*		477	Baseline	1	157282	Rebounder	Week 24 (169)	Y
				Week 4	30	106	Rebounder	Week 24 (169)	Y
				Week 8	56	171	Rebounder	Week 24 (169)	Y
				Week 16	114	<40 TND	Rebounder	Week 24 (169)	Y
				Week 24	169	70469	Rebounder	Week 24 (169)	Y
				Week 24	195	42	Rebounder	Week 24 (169)	Y
				Week 36	253	57794	Rebounder	Week 24 (169)	Y
				Week 36	276	<40 TND	Rebounder	Week 24 (169)	Y
				Week 48	337	137987	Rebounder	Week 24 (169)	Y
				Week 48	351	837	Rebounder	Week 24 (169)	Y
				Week 60	429	198629	Rebounder	Week 24 (169)	Y
				Week 72	477	15954	Rebounder	Week 24 (169)	Y
	P3011*			Baseline	1	91664	Rebounder	Week 36 (253)	Y
				Week 4	29	268	Rebounder	Week 36 (253)	Y
				Week 16	110	<40 TND	Rebounder	Week 36 (253)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3011*			Week 24	169	<40 TD	Rebounder	Week 36 (253)	Y
				Week 36	253	103	Rebounder	Week 36 (253)	Y
				Week 36	263	42	Rebounder	Week 36 (253)	Y
				Week 48	304	54	Rebounder	Week 36 (253)	Y
				Week 48	344	<40 TD	Rebounder	Week 36 (253)	Y
	P3012*			Baseline	1	22938	Rebounder	Week 8 (57)	Y
				Week 4	32	<40 TND	Rebounder	Week 8 (57)	Y
				Week 8	57	43	Rebounder	Week 8 (57)	Y
				Week 8	80	48	Rebounder	Week 8 (57)	Y
				Week 16	113	<40 TND	Rebounder	Week 8 (57)	Y
				Week 24	169	<40 TND	Rebounder	Week 8 (57)	Y
				Week 36	253	<40 TND	Rebounder	Week 8 (57)	Y
				Week 48	344	<40 TND	Rebounder	Week 8 (57)	Y
	P3013*			Baseline	1	128299	Rebounder	Week 36 (271)	Y
				Week 4	29	148	Rebounder	Week 36 (271)	Y
				Week 8	57	<40 TD	Rebounder	Week 36 (271)	Y
				Week 16	113	67	Rebounder	Week 36 (271)	Y
				Week 24	147	<40 TD	Rebounder	Week 36 (271)	Y
				Week 24	169	51	Rebounder	Week 36 (271)	Y
				Week 24	181	<40 TD	Rebounder	Week 36 (271)	Y
				Week 36	271	45	Rebounder	Week 36 (271)	Y
				Week 48	309	78	Rebounder	Week 36 (271)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3013*			Week 48	337	<40 TD	Rebounder	Week 36 (271)	Y
	P3014*			Baseline	1	21054	Rebounder	Week 48 (338)	
				Week 4	29	61	Rebounder	Week 48 (338)	
				Week 8	57	<40 TND	Rebounder	Week 48 (338)	
				Week 16	108	<40 TND	Rebounder	Week 48 (338)	
				Week 24	164	59	Rebounder	Week 48 (338)	
				Week 24	206	<40 TND	Rebounder	Week 48 (338)	
				Week 36	253	<40 TND	Rebounder	Week 48 (338)	
				Week 48	338	267	Rebounder	Week 48 (338)	
				Week 48	354	297	Rebounder	Week 48 (338)	
	P3015*			Baseline	1	17672	Rebounder	Week 24 (169)	Y
				Week 4	29	<40 TD	Rebounder	Week 24 (169)	Y
				Week 8	58	<40 TD	Rebounder	Week 24 (169)	Y
				Week 16	113	<40 TND	Rebounder	Week 24 (169)	Y
				Week 24	169	21670	Rebounder	Week 24 (169)	Y
				Week 36	239	18946	Rebounder	Week 24 (169)	Y
				Week 36	259	57	Rebounder	Week 24 (169)	Y
				Week 48	337	<40 TND	Rebounder	Week 24 (169)	Y
	P3016*	DISCONTINUED (LACK OF EFFICACY)	306	Baseline	1	67098	Rebounder	Week 16 (113)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3016*	DISCONTINUED (LACK OF EFFICACY)	306	Week 4	27	192	Rebounder	Week 16 (113)	
				Week 8	57	<40 TD	Rebounder	Week 16 (113)	
				Week 16	113	46	Rebounder	Week 16 (113)	
				Week 24	141	3661	Rebounder	Week 16 (113)	
				Week 24	147	151	Rebounder	Week 16 (113)	
				Week 24	169	45	Rebounder	Week 16 (113)	
				Week 36	253	1621	Rebounder	Week 16 (113)	
				Week 36	280	1516	Rebounder	Week 16 (113)	
				Week 48	307	18340	Rebounder	Week 16 (113)	
	P3017*	DISCONTINUED (WITHDRAWAL BY SUBJECT)	284	Baseline	1	142513	Non-responder	Week 24 (185)	
				Week 4	34	440	Non-responder	Week 24 (185)	
				Week 8	57	32285	Non-responder	Week 24 (185)	
				Week 16	115	128	Non-responder	Week 24 (185)	
				Week 24	169	806	Non-responder	Week 24 (185)	
				Week 24	185	366	Non-responder	Week 24 (185)	
				Week 36	218	392	Non-responder	Week 24 (185)	
				Week 36	253	5512	Non-responder	Week 24 (185)	
	P3018*			Baseline	1	16945	Rebounder	Week 36 (253)	Y
				Week 4	27	43	Rebounder	Week 36 (253)	Y
				Week 8	57	<40 TND	Rebounder	Week 36 (253)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3018*			Week 16	113	<40 TD	Rebounder	Week 36 (253)	Y
				Week 24	169	<40 TD	Rebounder	Week 36 (253)	Y
				Week 36	253	103	Rebounder	Week 36 (253)	Y
				Week 36	282	232	Rebounder	Week 36 (253)	Y
				Week 48	300	<40 TD	Rebounder	Week 36 (253)	Y
				Week 48	337	<40 TD	Rebounder	Week 36 (253)	Y
	P3019*			Baseline	1	9677	Rebounder	Week 36 (257)	Y
				Week 4	42	<40 TD	Rebounder	Week 36 (257)	Y
				Week 8	57	<40 TND	Rebounder	Week 36 (257)	Y
				Week 16	113	<40 TND	Rebounder	Week 36 (257)	Y
				Week 24	169	<40 TND	Rebounder	Week 36 (257)	Y
				Week 36	257	396	Rebounder	Week 36 (257)	Y
				Week 36	285	2180	Rebounder	Week 36 (257)	Y
				Week 48	337	3401	Rebounder	Week 36 (257)	Y
				Week 48	365	<40 TD	Rebounder	Week 36 (257)	Y
	P3020*			Baseline	1	43890	Rebounder	Week 24 (169)	Y
				Week 4	29	<40 TD	Rebounder	Week 24 (169)	Y
				Week 8	57	<40 TND	Rebounder	Week 24 (169)	Y
				Week 16	110	<40 TD	Rebounder	Week 24 (169)	Y
				Week 24	169	8908	Rebounder	Week 24 (169)	Y
				Week 24	190	1782	Rebounder	Week 24 (169)	Y
				Week 36	253	<40 TD	Rebounder	Week 24 (169)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3020*			Week 48	333	<40 TND	Rebounder	Week 24 (169)	Y
	P3021*	DISCONTINUED (WITHDRAWAL BY SUBJECT)	253	Baseline	1	43285	Rebounder	Week 16 (113)	Y
				Week 4	29	<40 TD	Rebounder	Week 16 (113)	Y
				Week 8	58	<40 TND	Rebounder	Week 16 (113)	Y
				Week 16	113	87	Rebounder	Week 16 (113)	Y
				Week 24	164	53	Rebounder	Week 16 (113)	Y
				Week 24	171	<40 TD	Rebounder	Week 16 (113)	Y
	P3022*			Baseline	1	446005	Non-responder	Week 24 (173)	
				Week 4	29	490	Non-responder	Week 24 (173)	
				Week 8	57	210	Non-responder	Week 24 (173)	
				Week 16	113	60	Non-responder	Week 24 (173)	
				Week 24	173	48	Non-responder	Week 24 (173)	
				Week 36	242	<40 TND	Non-responder	Week 24 (173)	
				Week 36	254	<40 TD	Non-responder	Week 24 (173)	
				Week 48	344	<40 TD	Non-responder	Week 24 (173)	
				Week 60	428	51	Non-responder	Week 24 (173)	
				Week 72	474	<40 TND	Non-responder	Week 24 (173)	
				Week 72	516	<40 TD	Non-responder	Week 24 (173)	
	P3023*			Baseline	1	1142389	Non-responder	Week 24 (190)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3023*			Week 4	29	986	Non-responder	Week 24 (190)	
				Week 8	58	362	Non-responder	Week 24 (190)	
				Week 16	113	96	Non-responder	Week 24 (190)	
				Week 24	163	138	Non-responder	Week 24 (190)	
				Week 24	185	163	Non-responder	Week 24 (190)	
				Week 24	190	52	Non-responder	Week 24 (190)	
				Week 36	253	48	Non-responder	Week 24 (190)	
				Week 48	343	<40 TND	Non-responder	Week 24 (190)	
				Week 60	430	<40 TD	Non-responder	Week 24 (190)	
	P3024*	DISCONTINUED (LACK OF EFFICACY)	253	Baseline	1	1921844	Non-responder	Week 24 (201)	
				Week 4	30	64947	Non-responder	Week 24 (201)	
				Week 8	58	644	Non-responder	Week 24 (201)	
				Week 16	115	2723	Non-responder	Week 24 (201)	
				Week 24	169	689	Non-responder	Week 24 (201)	
				Week 24	201	1816	Non-responder	Week 24 (201)	
				Week 36	235	1594	Non-responder	Week 24 (201)	
				Week 36	253	1816	Non-responder	Week 24 (201)	
				Week 36	267	<40 TD	Non-responder	Week 24 (201)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3025*	DISCONTINUED (NON-COMPLIANCE WITH STUDY DRUG)	349	Baseline	1	451643	Non-responder	Week 24 (168)	
				Week 4	29	262	Non-responder	Week 24 (168)	
				Week 8	57	73	Non-responder	Week 24 (168)	
				Week 16	113	69	Non-responder	Week 24 (168)	
				Week 24	168	46	Non-responder	Week 24 (168)	
				Week 36	218	<40 TND	Non-responder	Week 24 (168)	
				Week 36	253	<40 TD	Non-responder	Week 24 (168)	
				Week 48	342	131288	Non-responder	Week 24 (168)	
	P3026*			Baseline	1	1337149	Non-responder	Week 24 (168)	
				Week 4	28	358	Non-responder	Week 24 (168)	
				Week 8	54	272	Non-responder	Week 24 (168)	
				Week 16	112	96	Non-responder	Week 24 (168)	
				Week 24	168	113	Non-responder	Week 24 (168)	
				Week 36	214	<40 TND	Non-responder	Week 24 (168)	
				Week 36	238	<40 TND	Non-responder	Week 24 (168)	
				Week 48	326	<40 TD	Non-responder	Week 24 (168)	
				Week 60	413	<40 TD	Non-responder	Week 24 (168)	
	P3027*			Baseline	1	790660	Non-responder	Week 24 (196)	
				Week 4	27	211	Non-responder	Week 24 (196)	
				Week 8	57	71	Non-responder	Week 24 (196)	
				Week 16	114	45	Non-responder	Week 24 (196)	
				Week 24	170	84	Non-responder	Week 24 (196)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3027*			Week 24	196	179	Non-responder	Week 24 (196)	
				Week 36	211	68	Non-responder	Week 24 (196)	
				Week 36	259	58	Non-responder	Week 24 (196)	
				Week 48	335	<40 TD	Non-responder	Week 24 (196)	
				Week 60	421	<40 TD	Non-responder	Week 24 (196)	
	P3028*			Baseline	1	170351	Non-responder	Week 24 (169)	
				Week 4	30	263	Non-responder	Week 24 (169)	
				Week 8	58	146	Non-responder	Week 24 (169)	
				Week 16	111	55	Non-responder	Week 24 (169)	
				Week 24	169	57	Non-responder	Week 24 (169)	
				Week 36	212	<40 TND	Non-responder	Week 24 (169)	
				Week 36	254	<40 TD	Non-responder	Week 24 (169)	
				Week 48	338	52	Non-responder	Week 24 (169)	
				Week 60	428	47	Non-responder	Week 24 (169)	
	P3029*			Baseline	1	769751	Non-responder	Week 24 (169)	
				Week 4	29	534	Non-responder	Week 24 (169)	
				Week 8	57	144	Non-responder	Week 24 (169)	
				Week 16	113	53	Non-responder	Week 24 (169)	
				Week 24	169	59	Non-responder	Week 24 (169)	
				Week 36	239	<40 TND	Non-responder	Week 24 (169)	
				Week 36	253	<40 TD	Non-responder	Week 24 (169)	
				Week 48	337	<40 TD	Non-responder	Week 24 (169)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3029*			Week 60	421	<40 TD	Non-responder	Week 24 (169)	
	P3030*			Baseline	1	151718	Rebounder	Week 16 (113)	Y
				Week 4	28	559	Rebounder	Week 16 (113)	Y
				Week 8	57	<40 TD	Rebounder	Week 16 (113)	Y
				Week 16	113	41	Rebounder	Week 16 (113)	Y
				Week 24	169	51	Rebounder	Week 16 (113)	Y
				Week 36	252	<40 TD	Rebounder	Week 16 (113)	Y
				Week 48	336	<40 TD	Rebounder	Week 16 (113)	Y
				Week 60	422	46	Rebounder	Week 16 (113)	Y
				Week 60	440	<40 TD	Rebounder	Week 16 (113)	Y
	P3031*			Baseline	1	1182795	Non-responder	Week 24 (176)	
				Week 4	29	553	Non-responder	Week 24 (176)	
				Week 8	57	290	Non-responder	Week 24 (176)	
				Week 16	115	161	Non-responder	Week 24 (176)	
				Week 24	169	144	Non-responder	Week 24 (176)	
				Week 24	176	103	Non-responder	Week 24 (176)	
				Week 36	253	<40 TD	Non-responder	Week 24 (176)	
				Week 48	337	<40 TD	Non-responder	Week 24 (176)	
				Week 60	421	106	Non-responder	Week 24 (176)	

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3032*	DISCONTINUED (PHYSICIAN DECISION)	240	Baseline	-2	874664	Non-responder	Week 24 (192)	
				Week 4	27	229	Non-responder	Week 24 (192)	
				Week 8	58	148	Non-responder	Week 24 (192)	
				Week 16	111	81	Non-responder	Week 24 (192)	
				Week 24	167	159	Non-responder	Week 24 (192)	
				Week 24	192	198	Non-responder	Week 24 (192)	
				Week 36	240	404	Non-responder	Week 24 (192)	
				Week 36	250	134	Non-responder	Week 24 (192)	
	P3033*			Baseline	1	1094416	Non-responder	Week 24 (169)	
				Week 4	31	513	Non-responder	Week 24 (169)	
				Week 8	57	307	Non-responder	Week 24 (169)	
				Week 16	113	138	Non-responder	Week 24 (169)	
				Week 24	169	67	Non-responder	Week 24 (169)	
				Week 36	248	68	Non-responder	Week 24 (169)	
				Week 48	319	<40 TD	Non-responder	Week 24 (169)	
				Week 48	339	<40 TND	Non-responder	Week 24 (169)	
				Week 60	421	<40 TD	Non-responder	Week 24 (169)	
	P3034*		463	Baseline	1	3910386	Non-responder	Week 24 (183)	
				Week 4	29	993	Non-responder	Week 24 (183)	
				Week 8	57	737	Non-responder	Week 24 (183)	
				Week 16	113	195	Non-responder	Week 24 (183)	
				Week 24	169	108	Non-responder	Week 24 (183)	

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3034*		463	Week 24	183	109	Non-responder	Week 24 (183)	
				Week 36	249	115	Non-responder	Week 24 (183)	
				Week 48	337	42	Non-responder	Week 24 (183)	
				Week 60	421	1470	Non-responder	Week 24 (183)	
	P3035*			Baseline	1	194777	Rebounder	Week 8 (57)	Y
				Week 4	28	<40 TD	Rebounder	Week 8 (57)	Y
				Week 8	57	46	Rebounder	Week 8 (57)	Y
				Week 16	124	86	Rebounder	Week 8 (57)	Y
				Week 24	168	<40 TD	Rebounder	Week 8 (57)	Y
				Week 36	252	<40 TND	Rebounder	Week 8 (57)	Y
				Week 48	336	<40 TD	Rebounder	Week 8 (57)	Y
				Week 60	420	<40 TND	Rebounder	Week 8 (57)	Y
	P3036*			Baseline	1	1021044	Non-responder	Week 24 (178)	
				Week 4	29	510	Non-responder	Week 24 (178)	
				Week 8	57	388	Non-responder	Week 24 (178)	
				Week 16	113	220	Non-responder	Week 24 (178)	
				Week 24	169	146	Non-responder	Week 24 (178)	
				Week 24	178	85	Non-responder	Week 24 (178)	
				Week 36	254	46	Non-responder	Week 24 (178)	
				Week 48	340	299	Non-responder	Week 24 (178)	
				Week 48	374	18993	Non-responder	Week 24 (178)	
				Week 60	422	510510	Non-responder	Week 24 (178)	

＊新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3037*			Baseline	1	1041902	Non-responder	Week 24 (204)	
				Week 4	29	2058	Non-responder	Week 24 (204)	
				Week 8	57	648	Non-responder	Week 24 (204)	
				Week 16	113	345	Non-responder	Week 24 (204)	
				Week 24	169	169	Non-responder	Week 24 (204)	
				Week 24	204	297	Non-responder	Week 24 (204)	
				Week 36	253	77	Non-responder	Week 24 (204)	
				Week 48	337	<40 TD	Non-responder	Week 24 (204)	
				Week 60	421	81	Non-responder	Week 24 (204)	
	P3038*			Baseline	1	111693	Rebounder	Week 16 (113)	Y
				Week 4	29	74	Rebounder	Week 16 (113)	Y
				Week 8	57	<40 TD	Rebounder	Week 16 (113)	Y
				Week 16	113	103	Rebounder	Week 16 (113)	Y
				Week 24	149	105	Rebounder	Week 16 (113)	Y
				Week 24	170	<40 TD	Rebounder	Week 16 (113)	Y
				Week 36	253	<40 TD	Rebounder	Week 16 (113)	Y
				Week 48	337	<40 TD	Rebounder	Week 16 (113)	Y
	P3039*	DISCONTINUED (LACK OF EFFICACY)	259	Baseline	1	26345	Non-responder	Week 24 (176)	
				Week 4	29	13085	Non-responder	Week 24 (176)	
				Week 8	57	25552	Non-responder	Week 24 (176)	

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Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3039*	DISCONTINUED (LACK OF EFFICACY)	259	Week 16	114	5287	Non-responder	Week 24 (176)	
				Week 24	176	59161	Non-responder	Week 24 (176)	
				Week 36	259	20222	Non-responder	Week 24 (176)	
	P3040*	DISCONTINUED (LACK OF EFFICACY)	197	Baseline	1	150728	Non-responder	Week 24 (197)	
				Week 4	27	59	Non-responder	Week 24 (197)	
				Week 8	56	1057	Non-responder	Week 24 (197)	
				Week 16	112	3143	Non-responder	Week 24 (197)	
				Week 24	142	3287	Non-responder	Week 24 (197)	
				Week 24	168	10132	Non-responder	Week 24 (197)	
				Week 24	197	8049	Non-responder	Week 24 (197)	
	P3041*			Baseline	1	172261	Non-responder	Week 24 (169)	
				Week 4	29	220	Non-responder	Week 24 (169)	
				Week 8	57	70	Non-responder	Week 24 (169)	
				Week 16	114	42	Non-responder	Week 24 (169)	
				Week 24	169	63	Non-responder	Week 24 (169)	
				Week 36	253	<40 TD	Non-responder	Week 24 (169)	
				Week 48	337	<40 TND	Non-responder	Week 24 (169)	
	P3042*			Baseline	1	162041	Rebounder	Week 16 (113)	Y
				Week 4	30	104	Rebounder	Week 16 (113)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 1200 mg QD	P3042*			Week 8	58	<40 TD	Rebounder	Week 16 (113)	Y
				Week 16	113	41	Rebounder	Week 16 (113)	Y
				Week 16	127	56	Rebounder	Week 16 (113)	Y
				Week 24	169	<40 TND	Rebounder	Week 16 (113)	Y
				Week 36	253	<40 TD	Rebounder	Week 16 (113)	Y
				Week 48	337	<40 TD	Rebounder	Week 16 (113)	Y
Raltegravir 400 mg BID	P3043*	DISCONTINUED (WITHDRAWAL BY SUBJECT)	123	Baseline	1	13295	Rebounder	Week 16 (113)	
				Week 4	29	<40 TD	Rebounder	Week 16 (113)	
				Week 8	57	<40 TND	Rebounder	Week 16 (113)	
				Week 16	113	428	Rebounder	Week 16 (113)	
				Week 16	128	31405	Rebounder	Week 16 (113)	
	P3044*	DISCONTINUED (NON-COMPLIANCE WITH STUDY DRUG)	241	Baseline	1	18174	Rebounder	Week 24 (172)	
				Week 4	29	<40 TD	Rebounder	Week 24 (172)	
				Week 8	57	<40 TND	Rebounder	Week 24 (172)	
				Week 16	113	<40 TND	Rebounder	Week 24 (172)	
				Week 24	172	593	Rebounder	Week 24 (172)	
				Week 24	183	116	Rebounder	Week 24 (172)	

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3045*			Baseline	-1	17184	Rebounder	Week 24 (168)	Y
				Week 4	29	53	Rebounder	Week 24 (168)	Y
				Week 8	62	<40 TND	Rebounder	Week 24 (168)	Y
				Week 16	112	<40 TD	Rebounder	Week 24 (168)	Y
				Week 24	168	5296	Rebounder	Week 24 (168)	Y
				Week 24	184	270	Rebounder	Week 24 (168)	Y
				Week 36	237	<40 TND	Rebounder	Week 24 (168)	Y
				Week 36	272	<40 TND	Rebounder	Week 24 (168)	Y
				Week 48	336	<40 TD	Rebounder	Week 24 (168)	Y
	P3046*			Baseline	1	40107	Rebounder	Week 16 (114)	Y
				Week 4	34	<40 TD	Rebounder	Week 16 (114)	Y
				Week 8	57	<40 TD	Rebounder	Week 16 (114)	Y
				Week 16	114	122	Rebounder	Week 16 (114)	Y
				Week 16	135	323	Rebounder	Week 16 (114)	Y
				Week 24	169	69	Rebounder	Week 16 (114)	Y
				Week 36	253	47	Rebounder	Week 16 (114)	Y
				Week 48	331	40	Rebounder	Week 16 (114)	Y
				Week 48	371	<40 TND	Rebounder	Week 16 (114)	Y
	P3047*	DISCONTINUED (LACK OF EFFICACY)	231	Baseline	1	613133	Non-responder	Week 24 (197)	
				Week 4	29	826	Non-responder	Week 24 (197)	

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3047*	DISCONTINUED (LACK OF EFFICACY)	231	Week 8	57	269	Non-responder	Week 24 (197)	
				Week 16	113	196	Non-responder	Week 24 (197)	
				Week 24	190	113	Non-responder	Week 24 (197)	
				Week 24	197	110	Non-responder	Week 24 (197)	
				Week 36	232	186	Non-responder	Week 24 (197)	
	P3048*	DISCONTINUED (WITHDRAWAL BY SUBJECT)	347	Baseline	1	1466713	Non-responder	Week 24 (176)	
				Week 4	30	547	Non-responder	Week 24 (176)	
				Week 8	60	235	Non-responder	Week 24 (176)	
				Week 16	120	91	Non-responder	Week 24 (176)	
				Week 24	176	89	Non-responder	Week 24 (176)	
				Week 36	213	59	Non-responder	Week 24 (176)	
				Week 36	259	<40 TD	Non-responder	Week 24 (176)	
				Week 48	347	40	Non-responder	Week 24 (176)	
	P3049*			Baseline	1	566241	Non-responder	Week 24 (198)	
				Week 4	29	458	Non-responder	Week 24 (198)	
				Week 8	57	215	Non-responder	Week 24 (198)	
				Week 16	116	413	Non-responder	Week 24 (198)	
				Week 24	169	900	Non-responder	Week 24 (198)	
				Week 24	198	94	Non-responder	Week 24 (198)	
				Week 36	254	583	Non-responder	Week 24 (198)	

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Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3049*			Week 36	277	286	Non-responder	Week 24 (198)	
				Week 48	337	430	Non-responder	Week 24 (198)	
				Week 60	421	89	Non-responder	Week 24 (198)	
	P3050*			Baseline	1	335874	Rebounder	Week 48 (337)	Y
				Week 4	29	206	Rebounder	Week 48 (337)	Y
				Week 8	57	60	Rebounder	Week 48 (337)	Y
				Week 16	115	95	Rebounder	Week 48 (337)	Y
				Week 24	198	<40 TD	Rebounder	Week 48 (337)	Y
				Week 36	253	<40 TD	Rebounder	Week 48 (337)	Y
				Week 48	337	51	Rebounder	Week 48 (337)	Y
				Week 60	421	87	Rebounder	Week 48 (337)	Y
				Week 60	457	<40 TND	Rebounder	Week 48 (337)	Y
	P3051*			Baseline	1	464014	Non-responder	Week 24 (178)	
				Week 4	29	290	Non-responder	Week 24 (178)	
				Week 8	60	205	Non-responder	Week 24 (178)	
				Week 16	109	64	Non-responder	Week 24 (178)	
				Week 24	178	71	Non-responder	Week 24 (178)	
				Week 36	249	<40 TD	Non-responder	Week 24 (178)	
				Week 48	352	<40 TND	Non-responder	Week 24 (178)	
				Week 60	442	<40 TND	Non-responder	Week 24 (178)	
	P3052*			Baseline	1	222543	Rebounder	Week 16 (111)	Y

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Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3052*			Week 4	29	147	Rebounder	Week 16 (111)	Y
				Week 8	57	<40 TD	Rebounder	Week 16 (111)	Y
				Week 16	111	61	Rebounder	Week 16 (111)	Y
				Week 16	134	52	Rebounder	Week 16 (111)	Y
				Week 24	167	<40 TD	Rebounder	Week 16 (111)	Y
				Week 36	258	65	Rebounder	Week 16 (111)	Y
				Week 36	274	<40 TD	Rebounder	Week 16 (111)	Y
				Week 48	342	<40 TND	Rebounder	Week 16 (111)	Y
				Week 60	421	96	Rebounder	Week 16 (111)	Y
	P3053*			Baseline	1	302312	Non-responder	Week 24 (169)	
				Week 4	22	604	Non-responder	Week 24 (169)	
				Week 8	54	198	Non-responder	Week 24 (169)	
				Week 16	113	132	Non-responder	Week 24 (169)	
				Week 24	169	81	Non-responder	Week 24 (169)	
				Week 36	252	<40 TND	Non-responder	Week 24 (169)	
				Week 48	337	<40 TD	Non-responder	Week 24 (169)	
				Week 60	414	<40 TD	Non-responder	Week 24 (169)	
	P3054*			Baseline	1	155981	Rebounder	Week 24 (169)	Y
				Week 4	29	145	Rebounder	Week 24 (169)	Y
				Week 8	57	<40 TD	Rebounder	Week 24 (169)	Y
				Week 16	116	<40 TD	Rebounder	Week 24 (169)	Y
				Week 24	169	89	Rebounder	Week 24 (169)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3054*			Week 24	178	235	Rebounder	Week 24 (169)	Y
				Week 36	253	<40 TND	Rebounder	Week 24 (169)	Y
				Week 48	337	<40 TND	Rebounder	Week 24 (169)	Y
	P3055*			Baseline	1	251345	Non-responder	Week 24 (169)	
				Week 4	29	206	Non-responder	Week 24 (169)	
				Week 8	57	112	Non-responder	Week 24 (169)	
				Week 16	121	45	Non-responder	Week 24 (169)	
				Week 24	169	54	Non-responder	Week 24 (169)	
				Week 36	252	<40 TND	Non-responder	Week 24 (169)	
				Week 48	336	<40 TD	Non-responder	Week 24 (169)	
	P3056*			Baseline	1	291177	Non-responder	Week 24 (169)	
				Week 4	29	605	Non-responder	Week 24 (169)	
				Week 8	59	171	Non-responder	Week 24 (169)	
				Week 16	114	139	Non-responder	Week 24 (169)	
				Week 24	169	152	Non-responder	Week 24 (169)	
				Week 36	253	<40 TD	Non-responder	Week 24 (169)	
				Week 48	338	<40 TND	Non-responder	Week 24 (169)	
	P3057*			Baseline	1	1215511	Rebounder	Week 24 (169)	Y
				Week 4	29	381	Rebounder	Week 24 (169)	Y
				Week 8	57	77	Rebounder	Week 24 (169)	Y
				Week 16	113	<40 TD	Rebounder	Week 24 (169)	Y

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type†	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3057*			Week 24	169	52	Rebounder	Week 24 (169)	Y
				Week 24	190	72	Rebounder	Week 24 (169)	Y
				Week 36	253	<40 TD	Rebounder	Week 24 (169)	Y
				Week 48	337	44	Rebounder	Week 24 (169)	Y
				Week 60	382	<40 TND	Rebounder	Week 24 (169)	Y
	P3058*			Baseline	1	122160	Rebounder	Week 36 (253)	Y
				Week 4	20	327	Rebounder	Week 36 (253)	Y
				Week 8	57	<40 TD	Rebounder	Week 36 (253)	Y
				Week 16	114	<40 TD	Rebounder	Week 36 (253)	Y
				Week 24	169	<40 TD	Rebounder	Week 36 (253)	Y
				Week 36	253	40	Rebounder	Week 36 (253)	Y
				Week 48	342	85	Rebounder	Week 36 (253)	Y
				Week 60	381	<40 TD	Rebounder	Week 36 (253)	Y
	P3059*			Baseline	1	703153	Non-responder	Week 24 (162)	
				Week 4	27	459	Non-responder	Week 24 (162)	
				Week 8	54	130	Non-responder	Week 24 (162)	
				Week 16	110	61	Non-responder	Week 24 (162)	
				Week 24	162	90	Non-responder	Week 24 (162)	
				Week 36	243	<40 TND	Non-responder	Week 24 (162)	
				Week 48	334	<40 TND	Non-responder	Week 24 (162)	

* 新薬承認情報提供時に置き換え

Listing of Subjects with Protocol Defined Virologic Failure
Weeks 0-48

Treatment Group	Subject ID	Subject Status	Disc. Day	Visit	Relative Day	HIV RNA (copies/mL)	VF Type[†]	VF Week (Day)	Re-suppression
Raltegravir 400 mg BID	P3060*	DISCONTINUED (NON-COMPLIANCE WITH STUDY DRUG)	187	Baseline	1	222844	Non-responder	Week 24 (198)	
				Week 4	29	1547	Non-responder	Week 24 (198)	
				Week 8	58	4422	Non-responder	Week 24 (198)	
				Week 16	112	34716	Non-responder	Week 24 (198)	
				Week 24	170	92952	Non-responder	Week 24 (198)	
				Week 24	198	228213	Non-responder	Week 24 (198)	

TD: Target detected. TND: Target not detected.

[†] Virologic failure is defined as 1) Non-responder: Subjects who never achieved HIV RNA <40 copies/mL by Week 24, OR 2) Rebounder: Subjects who have two consecutive measurements of HIV-1 RNA ≥40 copies/mL at least one week apart after initial response of HIV-1 RNA <40 copies/mL.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 31

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type†	Viral Load (copies/mL) of Samples Sent for VR Testing‡	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM* for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	
RAL 1200 mg QD	P3005*	B	Week 48	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3008*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3009*	C	Week 16	RB	509	[None] (S)	0.99 (S)	[None] (S)	0.85 (S)	[None] (S)	0.97 (S)	No
	P3004*	B		DC	314282	[None] (S)	1.11 (S)	[None] (S)	1.19 (S)	[None] (S)	1.09 (S)	No
	P3010*	B	Week 24	RB	15954	[None] (S)	0.82 (S)	N.D.	N.D.	N.D.	N.D.	N/A
	P3061*	B		DC	11007	[None] (S)	1.01 (S)	[None] (S)	1.56 (S)	[None] (S)	1.23 (S)	No
	P3011*	B	Week 36	RB	54	[None] (S)	Failed (Failed)	[None] (S)	1.17 (S)	[None] (S)	0.88 (S)	No
	P3012*	Com-plex	Week 8	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3013*	B	Week 36	RB	78	[None] (S)	0.89 (S)	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	N/A
	P3014*	B	Week 48	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3015*	B	Week 24	RB	18946	[None] (S)	0.70 (S)	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	N/A
	P3016*	C	Week 16	RB	1516	[N155H, I203M] (R)	9.28 (R)	[M184V] (R)	>105.08 (R)	[None] (S)	0.58 (S)	Yes

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type†	Viral Load (copies/mL) of Samples Sent for VR Testing‡	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM* for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	
RAL 1200 mg QD	P3017*	B	Week 24	NR	14054	[None] (S)	1.24 (S)	[None] (S)	0.76 (S)	[None] (S)	0.88 (S)	No
	P3018*	B	Week 36	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3019*	C	Week 36	RB	2180	[Failed] (Failed)	Failed (Failed)	[None] (S)	1.13 (S)	[None] (S)	1.21 (S)	N/A
	P3020*	C	Week 24	RB	1782	[None] (S)	0.92 (S)	[V118I, M184M/I/V] (R)	>96.80 (R)	[None] (S)	0.43 (S)	Yes
	P3021*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3001*	B		DC	240524	[None] (S)	1.10 (S)	[None] (S)	1.50 (S)	[None] (S)	1.32 (S)	No
	P3022*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3023*	Com-plex	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3024*	B	Week 24	NR	1816	[L74M, E92Q] (R)	16.00 (R)	[M184V] (R)	>138.66 (R)	[None] (S)	0.53 (S)	Yes
			Week 24	NR	1816	[L74M, E92Q] (R)	19.00 (R)	[M184V] (R)	>53.50 (R)	[None] (S)	0.45 (S)	Yes
	P3025*	C	Week 24	NR	151154	[None] (S)	0.67 (S)	[None] (S)	1.02 (S)	[None] (S)	0.92 (S)	No
	P3026*	AE	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type[†]	Viral Load (copies/mL) of Samples Sent for VR Testing[‡]	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM[*] for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	
RAL 1200 mg QD	P3027*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3028*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3029*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3030*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3031*	F	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3032*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3033*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3034*	Com-plex	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3035*	C	Week 8	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3036*	B	Week 24	NR	18993	[N155H] (R)	13.00 (R)	[M184M/I/V] (R)	>87.95 (R)	[None] (S)	0.52 (S)	Yes
	P3037*	AB	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3038*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A

* 新薬承認情報提供時に置き換え

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type†	Viral Load (copies/mL) of Samples Sent for VR Testing‡	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM* for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	
RAL 1200 mg QD	P3062*	B		DC	665	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	N/A
	P3039*	B	Week 24	NR	20222	[Failed] (Failed)	Failed (Failed)	[V118I] (S)	1.04 (S)	[None] (S)	0.89 (S)	N/A
	P3040*	AE	Week 24	NR	3287	[V151I, N155H] (R)	Failed (Failed)	[M184V] (R)	>65.27 (R)	[None] (S)	0.37 (S)	Yes
	P3041*	A1	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3042*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3063*	B		DC	30132	[None] (S)	0.59 (S)	[None] (S)	0.98 (S)	[None] (S)	0.89 (S)	No
RAL 400 mg BID	P3043*	B	Week 16	RB		[Failed] (Failed)	Failed (Failed)	[None] (S)	1.61 (S)	[None] (S)	1.35 (S)	N/A
	P3044*	B	Week 24	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3045*	C	Week 24	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3046*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3064*	A1		DC	17730	[None] (S)	0.44 (S)	[None] (S)	0.79 (S)	[None] (S)	0.80 (S)	No
	P3047*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type[†]	Viral Load (copies/mL) of Samples Sent for VR Testing[‡]	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM[*] for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	Genotypic Resistance [Mutation] (G. Assessment[§])	Phenotypic Resistance Fold Change[‖] (P. Assessment[‖‖])	
RAL 400 mg BID	P3048*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3049*	Com-plex	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3050*	B	Week 48	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3051*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3052*	B	Week 16	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3053*	BF	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3054*	B	Week 24	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3055*	BF	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3056*	B	Week 24	NR	<40 TD	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	[Failed] (Failed)	Failed (Failed)	N/A
	P3057*	AE	Week 24	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3058*	BF	Week 36	RB		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A
	P3059*	B	Week 24	NR		N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N/A

* 新薬承認情報提供時に置き換え

Listing of Resistance Data for Subjects with Protocol Defined Virologic Failure and Early Discontinuation

Treatment Group	Subject ID	Sub-type	Week of VF	Viral Failure Type†	Viral Load (copies/mL) of Samples Sent for VR Testing‡	RAL Sensitivity		FTC Sensitivity		TDF Sensitivity		Presence of RAM* for Any Drug Known to Confer Resistance Present at VF
						Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	Genotypic Resistance [Mutation] (G. Assessment§)	Phenotypic Resistance Fold Change‖ (P. Assessment‖‖)	
RAL 400 mg BID	P3060*	B	Week 24	NR	228213	[None] (S)	0.86 (S)	[None] (S)	1.04 (S)	[None] (S)	1.16 (S)	No
	P3065*	B		DC	639244	[None] (S)	1.12 (S)	[None] (S)	1.22 (S)	[None] (S)	0.81 (S)	No

† Virologic failure (VF) Type:
Non-responder (NR): Subjects who never achieved HIV RNA <40 copies/mL by Week 24, OR
Rebounder (RB): Subjects who have two consecutive measurements of HIV-1 RNA ≥40 copies/mL at least one week apart after initial response of HIV-1 RNA <40 copies/mL.
Subjects who discontinued early (DC) and had resistance testing done.
‡ Resistance test: For subjects who meet the VF definition or discontinue early with HIV RNA value >500 copies/mL.
* RAM = Resistance-associated mutations to raltegravir (RAL) and/or emtricitabine (FTC) and/or tenofovir (TDF). [None]: No RAM identified by the Lab.
§ G. Assessment: Genotypic Assessment; S: Sensitive; RS: Reduced susceptibility.
‖ Fold Change is the IC50 fold change compared to the wild-type reference.
‖‖ P. Assessment: Phenotypic Assessment; R: Resistant; S: Sensitive; PS: Partially Sensitive; RS: Reduced susceptibility.
Failed: Failed resistance tests reported by the Lab.
N.D.: Test not done.
TD: Target detected. TND: Target not detected.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 32

Proportion of Subjects with Plasma HIV RNA <40 Copies/mL at Week 48 by Prognostic and Demographic Factors (Combined Baseline CD4 Subgroups) Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Total	472/501	94.2 (91.8, 96.1)	235/251	93.6 (89.9, 96.3)	0.6 (-2.8, 4.7)
Baseline Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	348/358	97.2 (94.9, 98.7)	173/177	97.7 (94.3, 99.4)	-0.5 (-3.2, 3.1)
>100,000 copies/mL	124/143	86.7 (80.0, 91.8)	62/74	83.8 (73.4, 91.3)	2.9 (-6.5, 14.1)
Baseline Plasma HIV RNA (copies/mL)					
≤500,000 copies/mL	456/479	95.2 (92.9, 96.9)	227/237	95.8 (92.4, 98.0)	-0.6 (-3.6, 3.1)
>500,000 copies/mL	16/22	72.7 (49.8, 89.3)	8/14	57.1 (28.9, 82.3)	15.6 (-15.6, 45.9)
Screening Plasma HIV RNA (copies/mL)					
≤100,000 copies/mL	345/357	96.6 (94.2, 98.3)	173/178	97.2 (93.6, 99.1)	-0.6 (-3.5, 3.3)
>100,000 copies/mL	127/144	88.2 (81.8, 93.0)	62/73	84.9 (74.6, 92.2)	3.3 (-5.8, 14.2)
Baseline CD4 Cell Counts (cells/mm^3)					
≤200 cells/mm^3	57/67	85.1 (74.3, 92.6)	29/33	87.9 (71.8, 96.6)	-2.8 (-16.0, 14.0)
>200 cells/mm^3	415/434	95.6 (93.2, 97.3)	206/218	94.5 (90.6, 97.1)	1.1 (-2.2, 5.3)
Hepatitis Status[‡]					
Hepatitis B and/or C Positive	13/13	100.0 (75.3, 100.0)	6/7	85.7 (42.1, 99.6)	14.3 (-11.7, 52.2)
Both Hepatitis B and C Negative	459/488	94.1 (91.6, 96.0)	229/244	93.9 (90.1, 96.5)	0.2 (-3.3, 4.3)
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use					
Yes	51/57	89.5 (78.5, 96.0)	37/39	94.9 (82.7, 99.4)	-5.4 (-17.0, 7.6)
No	421/444	94.8 (92.3, 96.7)	198/212	93.4 (89.2, 96.3)	1.4 (-2.2, 5.9)
Age (years)					
18 to 64	469/497	94.4 (92.0, 96.2)	232/248	93.5 (89.7, 96.3)	0.8 (-2.6, 5.0)
≥65	3/4	75.0 (19.4, 99.4)	3/3	100.0 (29.2, 100.0)	-25.0 (-72.3, 43.8)
Age (years)					
≤Median	242/257	94.2 (90.6, 96.7)	108/117	92.3 (85.9, 96.4)	1.9 (-3.2, 8.6)
>Median	230/244	94.3 (90.6, 96.8)	127/134	94.8 (89.5, 97.9)	-0.5 (-5.1, 5.1)

Proportion of Subjects with Plasma HIV RNA <40 Copies/mL at Week 48 by Prognostic and Demographic Factors (Combined Baseline CD4 Subgroups) Observed Failure Approach

Prognostic and Demographic Factors	Response				Difference in Percent Response (QD - BID)[†]
	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		
	n/N	% (95% CI)	n/N	% (95% CI)	% (95% CI)
Gender					
Male	393/415	94.7 (92.1, 96.6)	206/220	93.6 (89.6, 96.5)	1.1 (-2.6, 5.5)
Female	79/86	91.9 (83.9, 96.7)	29/31	93.5 (78.6, 99.2)	-1.7 (-11.1, 13.3)
Race					
American Indian or Alaska Native	3/3	100.0 (29.2, 100.0)	3/3	100.0 (29.2, 100.0)	0.0 (-60.6, 60.6)
Asian	76/81	93.8 (86.2, 98.0)	36/39	92.3 (79.1, 98.4)	1.5 (-7.7, 14.8)
Black or African American	83/93	89.2 (81.1, 94.7)	29/33	87.9 (71.8, 96.6)	1.4 (-9.7, 17.5)
Multiple	40/43	93.0 (80.9, 98.5)	13/14	92.9 (66.1, 99.8)	0.2 (-13.5, 25.4)
Native Hawaiian or Other Pacific Islander	0/0	N/A	1/1	100.0 (2.5, 100.0)	N/A
White	270/281	96.1 (93.1, 98.0)	153/161	95.0 (90.4, 97.8)	1.1 (-2.8, 5.9)
Ethnicity					
Hispanic or Latino	113/118	95.8 (90.4, 98.6)	48/49	98.0 (89.1, 99.9)	-2.2 (-7.9, 6.8)
Not Hispanic or Latino	336/358	93.9 (90.8, 96.1)	178/193	92.2 (87.5, 95.6)	1.6 (-2.6, 6.7)
Not Reported	17/19	89.5 (66.9, 98.7)	8/8	100.0 (63.1, 100.0)	-10.5 (-31.9, 24.0)
Unknown	6/6	100.0 (54.1, 100.0)	1/1	100.0 (2.5, 100.0)	0.0 (-42.8, 81.8)
Region					
Africa	39/41	95.1 (83.5, 99.4)	12/12	100.0 (73.5, 100.0)	-4.9 (-16.3, 20.0)
Asia/Pacific	79/84	94.0 (86.7, 98.0)	40/43	93.0 (80.9, 98.5)	1.0 (-7.7, 13.3)
Europe	183/190	96.3 (92.6, 98.5)	102/108	94.4 (88.3, 97.9)	1.9 (-2.9, 8.2)
Latin America	69/73	94.5 (86.6, 98.5)	26/26	100.0 (86.8, 100.0)	-5.5 (-13.3, 7.7)
North America	102/113	90.3 (83.2, 95.0)	55/62	88.7 (78.1, 95.3)	1.6 (-7.5, 12.7)
Viral Subtype					
Clade B	296/313	94.6 (91.4, 96.8)	164/175	93.7 (89.0, 96.8)	0.9 (-3.3, 5.9)
Non-Clade B	175/187	93.6 (89.1, 96.6)	69/74	93.2 (84.9, 97.8)	0.3 (-5.7, 8.9)
Missing	1/1	100.0 (2.5, 100.0)	2/2	100.0 (15.8, 100.0)	0.0 (-85.2, 74.2)

[†] The 95% CIs were calculated using Miettinen and Nurminen's method.

[‡] Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.

[§] Subjects who took at least one dose of PPI/H2 blocker during treatment period.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of subjects in each treatment group.

n = Number of subjects in each subcategory.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.3-qd1200: 33

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48 by Prognostic and Demographic Factors (Combined Baseline CD4 Subgroups) Observed Failure Approach

Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID][†] (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Total	499	407.3	232.0 (214.6, 249.4)	251	430.3	234.1 (212.8, 255.3)	-2.1 (-30.9, 26.7)
Baseline Plasma HIV RNA (copies/mL)							
≤100,000 copies/mL	358	431.0	214.4 (193.8, 235.1)	177	471.3	224.9 (199.2, 250.5)	-10.4 (-44.8, 24.0)
>100,000 copies/mL	141	347.2	276.4 (245.0, 307.9)	74	332.3	256.0 (217.8, 294.3)	20.4 (-30.9, 71.7)
Baseline Plasma HIV RNA (copies/mL)							
≤500,000 copies/mL	477	413.1	228.0 (210.7, 245.3)	237	444.2	237.4 (215.4, 259.5)	-9.5 (-38.5, 19.5)
>500,000 copies/mL	22	281.7	318.9 (191.3, 446.5)	14	194.9	176.7 (96.9, 256.5)	142.2 (-25.7, 310.1)
Screening Plasma HIV RNA (copies/mL)							
≤100,000 copies/mL	358	434.5	215.8 (195.0, 236.6)	177	475.6	226.4 (200.5, 252.4)	-10.6 (-45.3, 24.1)
>100,000 copies/mL	141	338.3	273.1 (242.0, 304.2)	74	322.1	252.3 (215.0, 289.6)	20.7 (-29.7, 71.2)
Baseline CD4 Cell Counts (cells/mm^3)							
≤200 cells/mm^3	66	128.4	209.2 (175.7, 242.7)	32	119.6	208.5 (171.8, 245.3)	0.6 (-53.4, 54.6)
>200 cells/mm^3	433	449.8	235.4 (216.0, 254.9)	219	475.7	237.8 (214.0, 261.6)	-2.3 (-34.4, 29.7)
Hepatitis Status[‡]							
Hepatitis B and/or C Positive	13	392.0	121.2 (31.9, 210.5)	7	422.1	145.9 (67.7, 224.0)	-24.7 (-152.9, 103.5)
Both Hepatitis B and C Negative	486	407.7	234.9 (217.2, 252.6)	244	430.6	236.6 (214.9, 258.3)	-1.7 (-30.9, 27.6)

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48 by Prognostic and Demographic Factors (Combined Baseline CD4 Subgroups) Observed Failure Approach

Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID][†] (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Concomitant[§] Proton Pump Inhibitors/H2 Blockers Use							
Yes	58	408.4	228.0 (159.4, 296.6)	39	445.3	225.3 (163.8, 286.8)	2.7 (-93.9, 99.3)
No	441	407.2	232.5 (214.8, 250.1)	212	427.6	235.7 (212.9, 258.4)	-3.2 (-33.1, 26.7)
Age (years)							
18 to 64	495	404.9	234.1 (217.5, 250.7)	248	429.3	235.0 (213.6, 256.5)	-0.9 (-28.8, 27.0)
≥65	4	698.0	-34.3 (-1252.4, 1183.9)	3	513.0	154.7 (-141.1, 450.5)	-188.9 (-1362.5, 984.6)
Age (years)							
≤Median	257	405.4	238.7 (216.7, 260.7)	118	424.9	231.4 (201.5, 261.2)	7.3 (-30.8, 45.5)
>Median	242	409.3	224.8 (197.4, 252.2)	133	435.2	236.4 (205.9, 266.9)	-11.6 (-54.8, 31.5)
Gender							
Male	414	426.5	235.3 (215.5, 255.1)	220	445.7	235.5 (212.3, 258.7)	-0.2 (-32.1, 31.8)
Female	85	313.7	215.6 (181.1, 250.1)	31	321.2	223.9 (170.8, 277.0)	-8.3 (-73.2, 56.6)
Race							
American Indian or Alaska Native	3	473.7	237.7 (-698.4, 1173.7)	3	452.0	225.7 (-52.4, 503.8)	12.0 (-618.1, 642.1)
Asian	81	371.2	259.6 (224.3, 294.9)	39	362.5	220.8 (172.5, 269.1)	38.8 (-21.5, 99.1)
Black or African American	93	351.4	212.9 (162.6, 263.2)	33	360.6	230.1 (173.6, 286.6)	-17.2 (-107.7, 73.3)
Multiple	42	376.2	239.6 (191.7, 287.5)	13	384.9	303.1 (223.6, 382.5)	-63.5 (-158.3, 31.4)
Native Hawaiian or Other Pacific Islander	0	N/A	N/A	1	334.0	72.0 (N/A)	N/A
White	280	440.3	229.1 (206.1, 252.0)	162	464.7	233.7 (205.4, 261.9)	-4.6 (-41.5, 32.4)

Change from Baseline in CD4 Cell Count (Cells/mm^3) at Week 48 by Prognostic and Demographic Factors (Combined Baseline CD4 Subgroups) Observed Failure Approach

Prognostic and Demographic Factors	Response						Difference in Mean Changes from Baseline [QD - BID]† (95% CI)
	Raltegravir 1200 mg QD			Raltegravir 400 mg BID			
	N	Baseline Mean	Mean Change from Baseline (95% CI)	N	Baseline Mean	Mean Change from Baseline (95% CI)	
Ethnicity							
Hispanic or Latino	119	427.3	248.7 (214.6, 282.7)	48	460.0	241.8 (188.6, 295.1)	6.8 (-56.1, 69.8)
Not Hispanic or Latino	355	400.5	219.7 (199.0, 240.3)	194	422.1	232.5 (208.4, 256.5)	-12.8 (-45.8, 20.3)
Not Reported	19	379.7	296.2 (207.0, 385.3)	8	485.3	244.4 (128.8, 360.0)	51.8 (-98.6, 202.1)
Unknown	6	498.0	423.5 (92.8, 754.2)	1	157.0	83.0 (N/A)	340.5 (-534.4, 1215.4)
Region							
Africa	41	272.4	216.0 (164.3, 267.7)	12	264.6	236.1 (158.3, 313.8)	-20.1 (-122.7, 82.5)
Asia/Pacific	84	354.8	250.4 (213.8, 287.0)	43	366.9	219.3 (175.3, 263.2)	31.1 (-28.4, 90.7)
Europe	189	447.6	229.1 (199.8, 258.4)	108	464.8	226.3 (192.8, 259.7)	2.9 (-43.2, 49.0)
Latin America	73	412.8	241.7 (202.5, 280.9)	26	403.3	281.8 (209.1, 354.4)	-40.1 (-117.7, 37.5)
North America	112	424.5	222.4 (178.4, 266.5)	62	457.7	237.5 (190.1, 284.9)	-15.1 (-83.6, 53.5)
Viral Subtype							
Clade B	311	423.6	231.6 (209.1, 254.1)	175	461.9	239.7 (213.3, 266.1)	-8.1 (-44.0, 27.7)
Non-Clade B	187	380.0	232.8 (205.0, 260.7)	74	349.8	225.8 (190.8, 260.8)	7.0 (-42.3, 56.3)
Missing	1	426.0	187.0 (N/A)	2	650.0	43.5 (-2898.0, 2985.0)	143.5 (-4951.3, 5238.3)

† The 95% CIs were based on t-distribution.
‡ Evidence of hepatitis B surface antigen and/or evidence of HCV RNA by polymerase chain reaction (PCR) quantitative test for hepatitis C Virus.
§ Subjects who took at least one dose of PPI/H2 blocker during treatment period.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.
N = Number of subjects in each treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

TABLE OF CONTENTS

LIST OF TABLES

This Application proposes the licensure of a new dose strength and dosing schedule for raltegravir (once daily administration of raltegravir [2x 600 mg tablets]). This section provides an overview of the safety profile of the proposed regimen of raltegravir 1200 mg QD (administered as 2 x 600 mg tablets).

One hundred and thirty-three (133) subjects (39 female; 94 male) received at least one dose of raltegravir 1200 mg or 1800 mg QD in six Phase 1 studies (PN290, PN291, PN293, PN812, PN823, PN824). Raltegravir QD was generally well tolerated after single doses of 1200 mg and multiple dose administration of 1200 mg and 1800 mg up to 28 days, when given alone or in combination with antacids, atazanavir or efavirenz. A summary of safety from these 6 Phase 1 studies can be found in ([Sec. 2.7.2.3.4]) ([Ref. 5.3.1.1: P290], [Ref. 5.3.1.1: P291], [Ref. 5.3.3.1: P293], [Ref. 5.3.2.2: P812], [Ref. 5.3.2.2: P823], [Ref. 5.3.2.2: P824]).

The primary evaluation of safety of raltegravir 1200 mg QD (2 x 600 mg tablets) occurred in a single Phase 3 study, Protocol 292, which is a multicenter, double-blind, randomized, active comparator-controlled clinical study that evaluated the safety and efficacy of raltegravir 1200 mg QD (2 x 600 mg tablets) versus raltegravir 400 mg BID, each in combination with TRUVADA™, in treatment-naïve HIV-1 infected subjects [Ref. 5.3.5.1: P292V01]. The primary efficacy endpoint of the study was to be measured at Treatment Week 48. Hence, this Application focuses on results of Protocol 292 through Treatment Week 48. The study will continue through Treatment Week 96.

Because there is only one Phase 3 study in support of this submission and the summary of this information is included within the Module 2.5, clinical overview, the Applicant has only included summary tables in this section, providing for a factual summarization of the information in addition to what is provided under Module 2.5 (see [Sec. 2.5.5]).

The enclosed tables describe findings through Treatment Week 48, with the exception of tables labeled “All Data Available”, which include data through 21-Dec-2015.

Table 2.7.4: 1

Extent of Exposure to Raltegravir by Dose Administered as Raltegravir 600 mg Tablet

Raltegravir	≤ 4 wks	> 4 wks to 8 wks	> 8 wks to 16 wks	> 16 wks to 24 wks	> 24 wks to 36 wks	> 36 wks to 48 wks	> 48 wks	Total Subjects	Duration Range	Mean Duration
Any Dose	4	5	10	10	8	63	431	531	9 to 515 days	385.9 days
600 mg	26	1	0	0	0	0	0	27	1 to 31 days	4.1 days
1200 mg	4	5	10	10	8	64	430	531	9 to 515 days	385.6 days
2400 mg	12	1	0	0	0	0	0	13	1 to 31 days	3.4 days

Each subject who received Raltegravir is counted once on the "Any Dose" row in the column that reflects the total duration of exposure to Raltegravir.

Each subject is counted again on one or more specific dose category rows that correspond to the actual dose(s) received. On each applicable specific dose row, the subject is counted once in the column that reflects the duration of exposure to that specific dose.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 2

Extent of Exposure to Raltegravir by Dose Administered as Raltegravir 400 mg Tablet

Raltegravir	≤ 4 wks	> 4 wks to 8 wks	> 8 wks to 16 wks	> 16 wks to 24 wks	> 24 wks to 36 wks	> 36 wks to 48 wks	> 48 wks	Total Subjects	Duration Range	Mean Duration
Any Dose	4	2	2	6	5	38	209	266	7 to 510 days	385.2 days
400 mg	103	4	0	0	0	0	0	107	1 to 51 days	5.5 days
800 mg	4	3	1	6	5	41	206	266	6 to 510 days	382.8 days
1200 mg	16	0	0	0	0	0	0	16	1 to 9 days	2.3 days
1600 mg	2	0	0	0	0	0	0	2	1 to 1 days	1.0 days

Each subject who received Raltegravir is counted once on the "Any Dose" row in the column that reflects the total duration of exposure to Raltegravir.

Each subject is counted again on one or more specific dose category rows that correspond to the actual dose(s) received. On each applicable specific dose row, the subject is counted once in the column that reflects the duration of exposure to that specific dose.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 3

Adverse Event Summary
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	439	(82.7)	231	(86.8)	670	(84.1)
with no adverse event	92	(17.3)	35	(13.2)	127	(15.9)
with drug-related† adverse events	130	(24.5)	68	(25.6)	198	(24.8)
with serious adverse events	31	(5.8)	25	(9.4)	56	(7.0)
with serious drug-related adverse events	1	(0.2)	2	(0.8)	3	(0.4)
who died	2	(0.4)	1	(0.4)	3	(0.4)
discontinued‡ due to an adverse event	4	(0.8)	6	(2.3)	10	(1.3)
discontinued due to a drug-related adverse event	0	(0.0)	2	(0.8)	2	(0.3)
discontinued due to a serious adverse event	3	(0.6)	2	(0.8)	5	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 4

Adverse Event Summary
Clinical Adverse Events
All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	440	(82.9)	233	(87.6)	673	(84.4)
with no adverse event	91	(17.1)	33	(12.4)	124	(15.6)
with drug-related† adverse events	132	(24.9)	68	(25.6)	200	(25.1)
with serious adverse events	35	(6.6)	30	(11.3)	65	(8.2)
with serious drug-related adverse events	1	(0.2)	2	(0.8)	3	(0.4)
who died	2	(0.4)	1	(0.4)	3	(0.4)
discontinued‡ due to an adverse event	4	(0.8)	6	(2.3)	10	(1.3)
discontinued due to a drug-related adverse event	0	(0.0)	2	(0.8)	2	(0.3)
discontinued due to a serious adverse event	3	(0.6)	2	(0.8)	5	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 5

Subjects With Clinical Adverse Events (Incidence ≥ 10% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n	(%)	n	(%)
Subjects in population	531		266	
with one or more adverse events	439	(82.7)	231	(86.8)
with no adverse events	92	(17.3)	35	(13.2)
Gastrointestinal disorders	**209**	**(39.4)**	**99**	**(37.2)**
Diarrhoea	58	(10.9)	30	(11.3)
Nausea	60	(11.3)	26	(9.8)
General disorders and administration site conditions	**84**	**(15.8)**	**49**	**(18.4)**
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**
Injury, poisoning and procedural complications	**57**	**(10.7)**	**28**	**(10.5)**
Musculoskeletal and connective tissue disorders	**89**	**(16.8)**	**36**	**(13.5)**
Nervous system disorders	**122**	**(23.0)**	**54**	**(20.3)**
Headache	71	(13.4)	29	(10.9)
Psychiatric disorders	**71**	**(13.4)**	**43**	**(16.2)**
Respiratory, thoracic and mediastinal disorders	**76**	**(14.3)**	**40**	**(15.0)**
Skin and subcutaneous tissue disorders	**101**	**(19.0)**	**63**	**(23.7)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 6

Analysis of Subjects With Clinical Adverse Events (Incidence ≥1% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)[†]
Subjects in population	531		266		
with one or more adverse events	439	(82.7)	231	(86.8)	-4.2 (-9.2, 1.3)
with no adverse events	92	(17.3)	35	(13.2)	4.2 (-1.3, 9.2)
Blood and lymphatic system disorders	**24**	**(4.5)**	**8**	**(3.0)**	**1.5 (-1.6, 4.1)**
Lymphadenopathy	15	(2.8)	5	(1.9)	0.9 (-1.7, 3.1)
Cardiac disorders	**5**	**(0.9)**	**3**	**(1.1)**	**-0.2 (-2.4, 1.3)**
Ear and labyrinth disorders	**14**	**(2.6)**	**8**	**(3.0)**	**-0.4 (-3.4, 1.9)**
Ear pain	5	(0.9)	4	(1.5)	-0.6 (-2.9, 1.0)
Eye disorders	**17**	**(3.2)**	**9**	**(3.4)**	**-0.2 (-3.3, 2.3)**
Gastrointestinal disorders	**209**	**(39.4)**	**99**	**(37.2)**	**2.1 (-5.1, 9.2)**
Abdominal discomfort	6	(1.1)	2	(0.8)	0.4 (-1.6, 1.8)
Abdominal distension	10	(1.9)	8	(3.0)	-1.1 (-4.1, 1.0)
Abdominal pain	40	(7.5)	11	(4.1)	3.4 (-0.2, 6.6)
Abdominal pain upper	13	(2.4)	4	(1.5)	0.9 (-1.5, 2.9)
Constipation	14	(2.6)	4	(1.5)	1.1 (-1.4, 3.1)
Diarrhoea	58	(10.9)	30	(11.3)	-0.4 (-5.3, 4.1)
Dyspepsia	12	(2.3)	7	(2.6)	-0.4 (-3.2, 1.8)
Flatulence	5	(0.9)	9	(3.4)	-2.4 (-5.4, -0.5)
Gastritis	3	(0.6)	6	(2.3)	-1.7 (-4.3, -0.1)
Gastrooesophageal reflux disease	8	(1.5)	8	(3.0)	-1.5 (-4.4, 0.5)
Haemorrhoids	6	(1.1)	3	(1.1)	0.0 (-2.2, 1.5)
Nausea	60	(11.3)	26	(9.8)	1.5 (-3.3, 5.8)
Proctitis	5	(0.9)	4	(1.5)	-0.6 (-2.9, 1.0)
Toothache	9	(1.7)	5	(1.9)	-0.2 (-2.8, 1.7)
Vomiting	35	(6.6)	15	(5.6)	1.0 (-2.9, 4.3)
General disorders and administration site conditions	**84**	**(15.8)**	**49**	**(18.4)**	**-2.6 (-8.5, 2.8)**
Asthenia	7	(1.3)	2	(0.8)	0.6 (-1.5, 2.1)
Chest pain	6	(1.1)	2	(0.8)	0.4 (-1.6, 1.8)
Chills	1	(0.2)	4	(1.5)	-1.3 (-3.6, -0.2)
Fatigue	33	(6.2)	16	(6.0)	0.2 (-3.7, 3.5)
Influenza like illness	9	(1.7)	11	(4.1)	-2.4 (-5.7, -0.1)
Pyrexia	21	(4.0)	11	(4.1)	-0.2 (-3.6, 2.6)
Thirst	1	(0.2)	3	(1.1)	-0.9 (-3.1, 0.1)
Hepatobiliary disorders	**6**	**(1.1)**	**3**	**(1.1)**	**0.0 (-2.2, 1.5)**

Analysis of Subjects With Clinical Adverse Events (Incidence ≥1% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)[†]
Immune system disorders	**9**	**(1.7)**	**0**	**(0.0)**	**1.7 (0.3, 3.2)**
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**	**-5.4 (-12.6, 2.0)**
Acarodermatitis	3	(0.6)	3	(1.1)	-0.6 (-2.7, 0.7)
Bronchitis	17	(3.2)	10	(3.8)	-0.6 (-3.8, 2.0)
Cellulitis	4	(0.8)	4	(1.5)	-0.8 (-3.1, 0.7)
Chlamydial infection	4	(0.8)	5	(1.9)	-1.1 (-3.6, 0.4)
Conjunctivitis	6	(1.1)	4	(1.5)	-0.4 (-2.8, 1.2)
Ear infection	6	(1.1)	2	(0.8)	0.4 (-1.6, 1.8)
Folliculitis	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Furuncle	2	(0.4)	4	(1.5)	-1.1 (-3.5, 0.2)
Gastroenteritis	16	(3.0)	11	(4.1)	-1.1 (-4.5, 1.5)
Genital herpes	1	(0.2)	4	(1.5)	-1.3 (-3.6, -0.2)
Gonorrhoea	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Herpes simplex	3	(0.6)	4	(1.5)	-0.9 (-3.3, 0.4)
Herpes zoster	10	(1.9)	3	(1.1)	0.8 (-1.5, 2.5)
Infected bite	1	(0.2)	3	(1.1)	-0.9 (-3.1, 0.1)
Influenza	18	(3.4)	12	(4.5)	-1.1 (-4.6, 1.6)
Lower respiratory tract infection	6	(1.1)	1	(0.4)	0.8 (-1.0, 2.1)
Nasopharyngitis	44	(8.3)	22	(8.3)	0.0 (-4.4, 3.9)
Oral herpes	8	(1.5)	3	(1.1)	0.4 (-1.9, 2.0)
Otitis media	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Pharyngitis	14	(2.6)	8	(3.0)	-0.4 (-3.4, 1.9)
Proctitis chlamydial	4	(0.8)	3	(1.1)	-0.4 (-2.6, 1.0)
Respiratory tract infection	6	(1.1)	2	(0.8)	0.4 (-1.6, 1.8)
Respiratory tract infection viral	4	(0.8)	4	(1.5)	-0.8 (-3.1, 0.7)
Rhinitis	9	(1.7)	5	(1.9)	-0.2 (-2.8, 1.7)
Sinusitis	6	(1.1)	5	(1.9)	-0.7 (-3.3, 0.9)
Syphilis	14	(2.6)	14	(5.3)	-2.6 (-6.2, 0.1)
Tonsillitis	13	(2.4)	6	(2.3)	0.2 (-2.6, 2.3)
Tooth infection	7	(1.3)	0	(0.0)	1.3 (-0.1, 2.7)
Upper respiratory tract infection	40	(7.5)	19	(7.1)	0.4 (-3.8, 4.0)
Urethritis	9	(1.7)	7	(2.6)	-0.9 (-3.8, 1.1)
Urinary tract infection	11	(2.1)	3	(1.1)	0.9 (-1.3, 2.8)
Viral infection	4	(0.8)	3	(1.1)	-0.4 (-2.6, 1.0)
Injury, poisoning and procedural complications	**57**	**(10.7)**	**28**	**(10.5)**	**0.2 (-4.7, 4.5)**
Accidental overdose	22	(4.1)	10	(3.8)	0.4 (-2.9, 3.1)
Procedural pain	1	(0.2)	3	(1.1)	-0.9 (-3.1, 0.1)
Investigations	**12**	**(2.3)**	**5**	**(1.9)**	**0.4 (-2.2, 2.4)**
Weight increased	2	(0.4)	3	(1.1)	-0.8 (-2.9, 0.4)

Analysis of Subjects With Clinical Adverse Events (Incidence ≥1% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)[†]
Metabolism and nutrition disorders	**27**	**(5.1)**	**13**	**(4.9)**	**0.2 (-3.4, 3.2)**
Decreased appetite	14	(2.6)	0	(0.0)	2.6 (1.2, 4.4)
Vitamin D deficiency	4	(0.8)	5	(1.9)	-1.1 (-3.6, 0.4)
Musculoskeletal and connective tissue disorders	**89**	**(16.8)**	**36**	**(13.5)**	**3.2 (-2.2, 8.2)**
Arthralgia	16	(3.0)	6	(2.3)	0.8 (-2.0, 3.0)
Back pain	24	(4.5)	8	(3.0)	1.5 (-1.6, 4.1)
Musculoskeletal pain	7	(1.3)	5	(1.9)	-0.6 (-3.1, 1.2)
Myalgia	19	(3.6)	7	(2.6)	0.9 (-2.0, 3.4)
Neck pain	7	(1.3)	2	(0.8)	0.6 (-1.5, 2.1)
Pain in extremity	11	(2.1)	4	(1.5)	0.6 (-1.9, 2.4)
Tendonitis	2	(0.4)	3	(1.1)	-0.8 (-2.9, 0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**25**	**(4.7)**	**10**	**(3.8)**	**0.9 (-2.4, 3.7)**
Anogenital warts	16	(3.0)	2	(0.8)	2.3 (0.1, 4.2)
Nervous system disorders	**122**	**(23.0)**	**54**	**(20.3)**	**2.7 (-3.6, 8.5)**
Dizziness	24	(4.5)	12	(4.5)	0.0 (-3.5, 2.9)
Headache	71	(13.4)	29	(10.9)	2.5 (-2.6, 7.0)
Hypoaesthesia	2	(0.4)	5	(1.9)	-1.5 (-4.0, -0.1)
Somnolence	10	(1.9)	2	(0.8)	1.1 (-0.9, 2.8)
Syncope	4	(0.8)	3	(1.1)	-0.4 (-2.6, 1.0)
Psychiatric disorders	**71**	**(13.4)**	**43**	**(16.2)**	**-2.8 (-8.4, 2.3)**
Abnormal dreams	15	(2.8)	7	(2.6)	0.2 (-2.7, 2.5)
Anxiety	11	(2.1)	4	(1.5)	0.6 (-1.9, 2.4)
Depression	14	(2.6)	11	(4.1)	-1.5 (-4.8, 1.0)
Insomnia	21	(4.0)	13	(4.9)	-0.9 (-4.5, 1.9)
Irritability	1	(0.2)	3	(1.1)	-0.9 (-3.1, 0.1)
Renal and urinary disorders	**13**	**(2.4)**	**6**	**(2.3)**	**0.2 (-2.6, 2.3)**
Reproductive system and breast disorders	**35**	**(6.6)**	**9**	**(3.4)**	**3.2 (-0.2, 6.2)**
Respiratory, thoracic and mediastinal disorders	**76**	**(14.3)**	**40**	**(15.0)**	**-0.7 (-6.2, 4.3)**
Cough	28	(5.3)	14	(5.3)	0.0 (-3.7, 3.1)
Epistaxis	6	(1.1)	1	(0.4)	0.8 (-1.0, 2.1)
Nasal congestion	6	(1.1)	6	(2.3)	-1.1 (-3.8, 0.6)
Oropharyngeal pain	20	(3.8)	9	(3.4)	0.4 (-2.8, 3.0)

Analysis of Subjects With Clinical Adverse Events (Incidence ≥1% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)[†]
Respiratory, thoracic and mediastinal disorders	**76**	**(14.3)**	**40**	**(15.0)**	**-0.7 (-6.2, 4.3)**
Rhinitis allergic	15	(2.8)	6	(2.3)	0.6 (-2.2, 2.8)
Rhinorrhoea	8	(1.5)	2	(0.8)	0.8 (-1.3, 2.3)
Sinus congestion	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Skin and subcutaneous tissue disorders	**101**	**(19.0)**	**63**	**(23.7)**	**-4.7 (-11.0, 1.3)**
Acne	10	(1.9)	3	(1.1)	0.8 (-1.5, 2.5)
Dermatitis	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Dry skin	6	(1.1)	3	(1.1)	0.0 (-2.2, 1.5)
Eczema	7	(1.3)	2	(0.8)	0.6 (-1.5, 2.1)
Night sweats	1	(0.2)	3	(1.1)	-0.9 (-3.1, 0.1)
Pruritus	15	(2.8)	15	(5.6)	-2.8 (-6.5, -0.0)
Rash	23	(4.3)	11	(4.1)	0.2 (-3.2, 3.0)
Rash papular	8	(1.5)	4	(1.5)	0.0 (-2.4, 1.7)
Seborrhoeic dermatitis	5	(0.9)	3	(1.1)	-0.2 (-2.4, 1.3)
Skin lesion	2	(0.4)	3	(1.1)	-0.8 (-2.9, 0.4)
Vascular disorders	**25**	**(4.7)**	**11**	**(4.1)**	**0.6 (-2.9, 3.4)**
Hypertension	16	(3.0)	7	(2.6)	0.4 (-2.5, 2.7)

[†] Based on Miettinen & Nurminen method.

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Estimated differences and confidence intervals are provided in accordance with the statistical analysis plan.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 7

Subjects With Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	439	(82.7)	231	(86.8)	670	(84.1)
with no adverse events	92	(17.3)	35	(13.2)	127	(15.9)
Blood and lymphatic system disorders	**24**	**(4.5)**	**8**	**(3.0)**	**32**	**(4.0)**
Anaemia	4	(0.8)	2	(0.8)	6	(0.8)
Lymphadenitis	1	(0.2)	0	(0.0)	1	(0.1)
Lymphadenopathy	15	(2.8)	5	(1.9)	20	(2.5)
Neutropenia	1	(0.2)	0	(0.0)	1	(0.1)
Splenomegaly	1	(0.2)	0	(0.0)	1	(0.1)
Spontaneous haematoma	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	1	(0.2)	1	(0.4)	2	(0.3)
Cardiac disorders	**5**	**(0.9)**	**3**	**(1.1)**	**8**	**(1.0)**
Acute coronary syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Cardiovascular disorder	0	(0.0)	1	(0.4)	1	(0.1)
Palpitations	1	(0.2)	1	(0.4)	2	(0.3)
Tachycardia	2	(0.4)	1	(0.4)	3	(0.4)
Ventricular tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Congenital, familial and genetic disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
Glucose-6-phosphate dehydrogenase deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Hydrocele	1	(0.2)	0	(0.0)	1	(0.1)
Ear and labyrinth disorders	**14**	**(2.6)**	**8**	**(3.0)**	**22**	**(2.8)**
Cerumen impaction	2	(0.4)	1	(0.4)	3	(0.4)
Ear canal erythema	1	(0.2)	0	(0.0)	1	(0.1)
Ear discomfort	2	(0.4)	0	(0.0)	2	(0.3)
Ear pain	5	(0.9)	4	(1.5)	9	(1.1)
Eustachian tube dysfunction	1	(0.2)	0	(0.0)	1	(0.1)
Excessive cerumen production	1	(0.2)	0	(0.0)	1	(0.1)
Hypoacusis	0	(0.0)	1	(0.4)	1	(0.1)
Middle ear effusion	1	(0.2)	0	(0.0)	1	(0.1)
Tinnitus	1	(0.2)	1	(0.4)	2	(0.3)
Tympanic membrane perforation	1	(0.2)	0	(0.0)	1	(0.1)
Vertigo	1	(0.2)	2	(0.8)	3	(0.4)
Endocrine disorders	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
Androgen deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Autoimmune thyroiditis	1	(0.2)	0	(0.0)	1	(0.1)
Hypothyroidism	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Eye disorders	**17**	**(3.2)**	**9**	**(3.4)**	**26**	**(3.3)**
Cataract	1	(0.2)	2	(0.8)	3	(0.4)
Chorioretinopathy	1	(0.2)	0	(0.0)	1	(0.1)
Conjunctival haemorrhage	0	(0.0)	1	(0.4)	1	(0.1)
Conjunctivitis allergic	1	(0.2)	0	(0.0)	1	(0.1)
Dry eye	2	(0.4)	0	(0.0)	2	(0.3)
Eye irritation	1	(0.2)	1	(0.4)	2	(0.3)
Eye pain	0	(0.0)	1	(0.4)	1	(0.1)
Eye pruritus	3	(0.6)	1	(0.4)	4	(0.5)
Eyelid disorder	2	(0.4)	0	(0.0)	2	(0.3)
Eyelid myoclonus	0	(0.0)	1	(0.4)	1	(0.1)
Keratitis	0	(0.0)	1	(0.4)	1	(0.1)
Ocular icterus	1	(0.2)	0	(0.0)	1	(0.1)
Presbyopia	1	(0.2)	0	(0.0)	1	(0.1)
Pterygium	1	(0.2)	1	(0.4)	2	(0.3)
Retinopathy hypertensive	1	(0.2)	0	(0.0)	1	(0.1)
Strabismus	1	(0.2)	0	(0.0)	1	(0.1)
Vision blurred	1	(0.2)	2	(0.8)	3	(0.4)
Visual impairment	2	(0.4)	0	(0.0)	2	(0.3)
Vitreous floaters	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**209**	**(39.4)**	**99**	**(37.2)**	**308**	**(38.6)**
Abdominal discomfort	6	(1.1)	2	(0.8)	8	(1.0)
Abdominal distension	10	(1.9)	8	(3.0)	18	(2.3)
Abdominal hernia	1	(0.2)	1	(0.4)	2	(0.3)
Abdominal pain	40	(7.5)	11	(4.1)	51	(6.4)
Abdominal pain lower	3	(0.6)	0	(0.0)	3	(0.4)
Abdominal pain upper	13	(2.4)	4	(1.5)	17	(2.1)
Abdominal tenderness	1	(0.2)	0	(0.0)	1	(0.1)
Abnormal faeces	1	(0.2)	0	(0.0)	1	(0.1)
Anal fissure	4	(0.8)	0	(0.0)	4	(0.5)
Anal fistula	0	(0.0)	1	(0.4)	1	(0.1)
Anal pruritus	1	(0.2)	0	(0.0)	1	(0.1)
Anal skin tags	1	(0.2)	0	(0.0)	1	(0.1)
Anogenital dysplasia	1	(0.2)	1	(0.4)	2	(0.3)
Anorectal discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Aphthous ulcer	5	(0.9)	1	(0.4)	6	(0.8)
Cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chronic gastritis	0	(0.0)	2	(0.8)	2	(0.3)
Colitis	1	(0.2)	0	(0.0)	1	(0.1)
Constipation	14	(2.6)	4	(1.5)	18	(2.3)
Dental caries	3	(0.6)	0	(0.0)	3	(0.4)

Subjects With Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**209**	**(39.4)**	**99**	**(37.2)**	**308**	**(38.6)**
Diarrhoea	58	(10.9)	30	(11.3)	88	(11.0)
Diverticulum	2	(0.4)	0	(0.0)	2	(0.3)
Dry mouth	4	(0.8)	2	(0.8)	6	(0.8)
Dyspepsia	12	(2.3)	7	(2.6)	19	(2.4)
Dysphagia	1	(0.2)	0	(0.0)	1	(0.1)
Enteritis	1	(0.2)	0	(0.0)	1	(0.1)
Epigastric discomfort	2	(0.4)	0	(0.0)	2	(0.3)
Eructation	1	(0.2)	0	(0.0)	1	(0.1)
Faecaloma	0	(0.0)	1	(0.4)	1	(0.1)
Faeces hard	1	(0.2)	1	(0.4)	2	(0.3)
Faeces soft	1	(0.2)	1	(0.4)	2	(0.3)
Flatulence	5	(0.9)	9	(3.4)	14	(1.8)
Food poisoning	0	(0.0)	2	(0.8)	2	(0.3)
Frequent bowel movements	1	(0.2)	1	(0.4)	2	(0.3)
Gastric disorder	1	(0.2)	0	(0.0)	1	(0.1)
Gastric ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	3	(0.6)	6	(2.3)	9	(1.1)
Gastrointestinal disorder	2	(0.4)	0	(0.0)	2	(0.3)
Gastrointestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Gastrooesophageal reflux disease	8	(1.5)	8	(3.0)	16	(2.0)
Gingival bleeding	1	(0.2)	0	(0.0)	1	(0.1)
Glossodynia	1	(0.2)	0	(0.0)	1	(0.1)
Haemorrhoidal haemorrhage	1	(0.2)	1	(0.4)	2	(0.3)
Haemorrhoids	6	(1.1)	3	(1.1)	9	(1.1)
Hyperchlorhydria	0	(0.0)	1	(0.4)	1	(0.1)
Hypoaesthesia oral	1	(0.2)	0	(0.0)	1	(0.1)
Inguinal hernia	1	(0.2)	1	(0.4)	2	(0.3)
Irritable bowel syndrome	3	(0.6)	0	(0.0)	3	(0.4)
Mouth ulceration	1	(0.2)	1	(0.4)	2	(0.3)
Mucous stools	0	(0.0)	1	(0.4)	1	(0.1)
Nausea	60	(11.3)	26	(9.8)	86	(10.8)
Noninfective gingivitis	1	(0.2)	0	(0.0)	1	(0.1)
Odynophagia	4	(0.8)	1	(0.4)	5	(0.6)
Oral pain	2	(0.4)	1	(0.4)	3	(0.4)
Painful defaecation	0	(0.0)	1	(0.4)	1	(0.1)
Pancreatitis	1	(0.2)	0	(0.0)	1	(0.1)
Pancreatitis chronic	1	(0.2)	0	(0.0)	1	(0.1)
Peptic ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Proctalgia	3	(0.6)	0	(0.0)	3	(0.4)
Proctitis	5	(0.9)	4	(1.5)	9	(1.1)
Rectal discharge	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**209**	**(39.4)**	**99**	**(37.2)**	**308**	**(38.6)**
Rectal haemorrhage	4	(0.8)	0	(0.0)	4	(0.5)
Rectal stenosis	1	(0.2)	0	(0.0)	1	(0.1)
Rectal tenesmus	1	(0.2)	1	(0.4)	2	(0.3)
Stomatitis	1	(0.2)	1	(0.4)	2	(0.3)
Tongue disorder	0	(0.0)	1	(0.4)	1	(0.1)
Tongue ulceration	0	(0.0)	1	(0.4)	1	(0.1)
Tooth disorder	1	(0.2)	0	(0.0)	1	(0.1)
Tooth impacted	1	(0.2)	0	(0.0)	1	(0.1)
Toothache	9	(1.7)	5	(1.9)	14	(1.8)
Varices oesophageal	1	(0.2)	0	(0.0)	1	(0.1)
Vomiting	35	(6.6)	15	(5.6)	50	(6.3)
General disorders and administration site conditions	**84**	**(15.8)**	**49**	**(18.4)**	**133**	**(16.7)**
Asthenia	7	(1.3)	2	(0.8)	9	(1.1)
Calcinosis	0	(0.0)	1	(0.4)	1	(0.1)
Chest discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Chest pain	6	(1.1)	2	(0.8)	8	(1.0)
Chills	1	(0.2)	4	(1.5)	5	(0.6)
Drug ineffective	0	(0.0)	1	(0.4)	1	(0.1)
Drug withdrawal syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Facial pain	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	33	(6.2)	16	(6.0)	49	(6.1)
Feeling abnormal	0	(0.0)	1	(0.4)	1	(0.1)
Feeling hot	2	(0.4)	0	(0.0)	2	(0.3)
Hangover	1	(0.2)	0	(0.0)	1	(0.1)
Hunger	0	(0.0)	1	(0.4)	1	(0.1)
Inflammation	0	(0.0)	1	(0.4)	1	(0.1)
Influenza like illness	9	(1.7)	11	(4.1)	20	(2.5)
Local swelling	1	(0.2)	0	(0.0)	1	(0.1)
Malaise	0	(0.0)	1	(0.4)	1	(0.1)
Non-cardiac chest pain	0	(0.0)	1	(0.4)	1	(0.1)
Oedema peripheral	2	(0.4)	0	(0.0)	2	(0.3)
Pain	1	(0.2)	2	(0.8)	3	(0.4)
Peripheral swelling	3	(0.6)	1	(0.4)	4	(0.5)
Pyrexia	21	(4.0)	11	(4.1)	32	(4.0)
Sluggishness	0	(0.0)	1	(0.4)	1	(0.1)
Thirst	1	(0.2)	3	(1.1)	4	(0.5)
Xerosis	1	(0.2)	1	(0.4)	2	(0.3)
Hepatobiliary disorders	**6**	**(1.1)**	**3**	**(1.1)**	**9**	**(1.1)**

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Hepatobiliary disorders	**6**	**(1.1)**	**3**	**(1.1)**	**9**	**(1.1)**
Cholecystitis	2	(0.4)	0	(0.0)	2	(0.3)
Cholestasis	0	(0.0)	1	(0.4)	1	(0.1)
Hepatic steatosis	3	(0.6)	1	(0.4)	4	(0.5)
Hepatitis	0	(0.0)	1	(0.4)	1	(0.1)
Hepatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Jaundice	1	(0.2)	0	(0.0)	1	(0.1)
Portal hypertension	1	(0.2)	0	(0.0)	1	(0.1)
Immune system disorders	**9**	**(1.7)**	**0**	**(0.0)**	**9**	**(1.1)**
Allergy to arthropod sting	1	(0.2)	0	(0.0)	1	(0.1)
Drug hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
House dust allergy	1	(0.2)	0	(0.0)	1	(0.1)
Immunosuppression	1	(0.2)	0	(0.0)	1	(0.1)
Seasonal allergy	5	(0.9)	0	(0.0)	5	(0.6)
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**	**421**	**(52.8)**
Abdominal wall abscess	1	(0.2)	0	(0.0)	1	(0.1)
Abscess	0	(0.0)	1	(0.4)	1	(0.1)
Abscess limb	0	(0.0)	1	(0.4)	1	(0.1)
Acarodermatitis	3	(0.6)	3	(1.1)	6	(0.8)
Acquired immunodeficiency syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Acute hepatitis C	1	(0.2)	0	(0.0)	1	(0.1)
Acute sinusitis	2	(0.4)	1	(0.4)	3	(0.4)
Anal abscess	2	(0.4)	1	(0.4)	3	(0.4)
Angular cheilitis	1	(0.2)	2	(0.8)	3	(0.4)
Anorectal human papilloma virus infection	0	(0.0)	1	(0.4)	1	(0.1)
Bacterial vaginosis	2	(0.4)	0	(0.0)	2	(0.3)
Bartholinitis	0	(0.0)	1	(0.4)	1	(0.1)
Blister infected	1	(0.2)	0	(0.0)	1	(0.1)
Body tinea	3	(0.6)	1	(0.4)	4	(0.5)
Breast abscess	1	(0.2)	0	(0.0)	1	(0.1)
Breast cellulitis	1	(0.2)	0	(0.0)	1	(0.1)
Bronchitis	17	(3.2)	10	(3.8)	27	(3.4)
Bronchitis bacterial	2	(0.4)	0	(0.0)	2	(0.3)
Bullous impetigo	1	(0.2)	0	(0.0)	1	(0.1)
Carbuncle	1	(0.2)	0	(0.0)	1	(0.1)
Cellulitis	4	(0.8)	4	(1.5)	8	(1.0)
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)	1	(0.1)
Cervicitis	1	(0.2)	0	(0.0)	1	(0.1)
Chest wall abscess	1	(0.2)	0	(0.0)	1	(0.1)
Chikungunya virus infection	2	(0.4)	2	(0.8)	4	(0.5)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**	**421**	**(52.8)**
Chlamydial infection	4	(0.8)	5	(1.9)	9	(1.1)
Clostridium difficile colitis	0	(0.0)	1	(0.4)	1	(0.1)
Conjunctivitis	6	(1.1)	4	(1.5)	10	(1.3)
Conjunctivitis viral	1	(0.2)	0	(0.0)	1	(0.1)
Cryptosporidiosis infection	0	(0.0)	1	(0.4)	1	(0.1)
Cystitis	1	(0.2)	0	(0.0)	1	(0.1)
Cytomegalovirus infection	1	(0.2)	0	(0.0)	1	(0.1)
Dengue fever	2	(0.4)	0	(0.0)	2	(0.3)
Diarrhoea infectious	2	(0.4)	1	(0.4)	3	(0.4)
Ear infection	6	(1.1)	2	(0.8)	8	(1.0)
Ear lobe infection	0	(0.0)	1	(0.4)	1	(0.1)
Epididymitis	4	(0.8)	1	(0.4)	5	(0.6)
Eye infection	1	(0.2)	0	(0.0)	1	(0.1)
Folliculitis	5	(0.9)	3	(1.1)	8	(1.0)
Fungal skin infection	3	(0.6)	2	(0.8)	5	(0.6)
Furuncle	2	(0.4)	4	(1.5)	6	(0.8)
Gastroenteritis	16	(3.0)	11	(4.1)	27	(3.4)
Gastroenteritis bacterial	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis norovirus	1	(0.2)	0	(0.0)	1	(0.1)
Gastroenteritis viral	2	(0.4)	0	(0.0)	2	(0.3)
Genital herpes	1	(0.2)	4	(1.5)	5	(0.6)
Genital herpes simplex	2	(0.4)	2	(0.8)	4	(0.5)
Genital herpes zoster	1	(0.2)	0	(0.0)	1	(0.1)
Genitourinary chlamydia infection	2	(0.4)	0	(0.0)	2	(0.3)
Genitourinary tract gonococcal infection	2	(0.4)	0	(0.0)	2	(0.3)
Giardiasis	1	(0.2)	1	(0.4)	2	(0.3)
Gingivitis	4	(0.8)	1	(0.4)	5	(0.6)
Gonorrhoea	5	(0.9)	3	(1.1)	8	(1.0)
Helicobacter infection	1	(0.2)	1	(0.4)	2	(0.3)
Hepatitis B	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis C	2	(0.4)	0	(0.0)	2	(0.3)
Herpangina	1	(0.2)	0	(0.0)	1	(0.1)
Herpes simplex	3	(0.6)	4	(1.5)	7	(0.9)
Herpes virus infection	0	(0.0)	1	(0.4)	1	(0.1)
Herpes zoster	10	(1.9)	3	(1.1)	13	(1.6)
Hordeolum	5	(0.9)	1	(0.4)	6	(0.8)
Impetigo	2	(0.4)	1	(0.4)	3	(0.4)
Infected bite	1	(0.2)	3	(1.1)	4	(0.5)
Influenza	18	(3.4)	12	(4.5)	30	(3.8)
Labyrinthitis	0	(0.0)	1	(0.4)	1	(0.1)
Laryngitis	2	(0.4)	2	(0.8)	4	(0.5)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**	**421**	**(52.8)**
Latent syphilis	2	(0.4)	2	(0.8)	4	(0.5)
Latent tuberculosis	1	(0.2)	1	(0.4)	2	(0.3)
Lice infestation	0	(0.0)	1	(0.4)	1	(0.1)
Localised infection	1	(0.2)	1	(0.4)	2	(0.3)
Lower respiratory tract infection	6	(1.1)	1	(0.4)	7	(0.9)
Lymphogranuloma venereum	1	(0.2)	1	(0.4)	2	(0.3)
Molluscum contagiosum	2	(0.4)	0	(0.0)	2	(0.3)
Nail infection	1	(0.2)	0	(0.0)	1	(0.1)
Nasopharyngitis	44	(8.3)	22	(8.3)	66	(8.3)
Oesophageal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Onychomycosis	5	(0.9)	2	(0.8)	7	(0.9)
Oral candidiasis	4	(0.8)	1	(0.4)	5	(0.6)
Oral fungal infection	1	(0.2)	0	(0.0)	1	(0.1)
Oral herpes	8	(1.5)	3	(1.1)	11	(1.4)
Orchitis	0	(0.0)	2	(0.8)	2	(0.3)
Oropharyngeal gonococcal infection	1	(0.2)	0	(0.0)	1	(0.1)
Osteomyelitis	0	(0.0)	1	(0.4)	1	(0.1)
Otitis externa	1	(0.2)	1	(0.4)	2	(0.3)
Otitis media	5	(0.9)	3	(1.1)	8	(1.0)
Otitis media acute	1	(0.2)	0	(0.0)	1	(0.1)
Parasitic gastroenteritis	0	(0.0)	1	(0.4)	1	(0.1)
Penile abscess	0	(0.0)	1	(0.4)	1	(0.1)
Perineal abscess	0	(0.0)	1	(0.4)	1	(0.1)
Periodontitis	2	(0.4)	2	(0.8)	4	(0.5)
Periorbital cellulitis	1	(0.2)	1	(0.4)	2	(0.3)
Pharyngitis	14	(2.6)	8	(3.0)	22	(2.8)
Pharyngitis bacterial	1	(0.2)	0	(0.0)	1	(0.1)
Pharyngitis streptococcal	1	(0.2)	2	(0.8)	3	(0.4)
Pharyngotonsillitis	0	(0.0)	1	(0.4)	1	(0.1)
Pitted keratolysis	1	(0.2)	0	(0.0)	1	(0.1)
Pneumocystis jirovecii pneumonia	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	4	(0.8)	2	(0.8)	6	(0.8)
Pneumonia bacterial	0	(0.0)	1	(0.4)	1	(0.1)
Primary syphilis	3	(0.6)	0	(0.0)	3	(0.4)
Proctitis chlamydial	4	(0.8)	3	(1.1)	7	(0.9)
Proctitis gonococcal	2	(0.4)	0	(0.0)	2	(0.3)
Pyoderma	0	(0.0)	1	(0.4)	1	(0.1)
Rash pustular	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory tract infection	6	(1.1)	2	(0.8)	8	(1.0)
Respiratory tract infection viral	4	(0.8)	4	(1.5)	8	(1.0)
Rhinitis	9	(1.7)	5	(1.9)	14	(1.8)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**271**	**(51.0)**	**150**	**(56.4)**	**421**	**(52.8)**
Secondary syphilis	3	(0.6)	1	(0.4)	4	(0.5)
Sepsis	1	(0.2)	0	(0.0)	1	(0.1)
Sexually transmitted disease	0	(0.0)	1	(0.4)	1	(0.1)
Shigella infection	0	(0.0)	1	(0.4)	1	(0.1)
Sinusitis	6	(1.1)	5	(1.9)	11	(1.4)
Skin bacterial infection	0	(0.0)	1	(0.4)	1	(0.1)
Skin candida	1	(0.2)	1	(0.4)	2	(0.3)
Skin infection	1	(0.2)	0	(0.0)	1	(0.1)
Spirochaetal infection	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	4	(0.8)	2	(0.8)	6	(0.8)
Syphilis	14	(2.6)	14	(5.3)	28	(3.5)
Tinea infection	2	(0.4)	0	(0.0)	2	(0.3)
Tinea pedis	2	(0.4)	2	(0.8)	4	(0.5)
Tinea versicolour	1	(0.2)	1	(0.4)	2	(0.3)
Tonsillitis	13	(2.4)	6	(2.3)	19	(2.4)
Tonsillitis bacterial	2	(0.4)	0	(0.0)	2	(0.3)
Tooth abscess	3	(0.6)	1	(0.4)	4	(0.5)
Tooth infection	7	(1.3)	0	(0.0)	7	(0.9)
Tuberculosis	2	(0.4)	2	(0.8)	4	(0.5)
Upper respiratory tract infection	40	(7.5)	19	(7.1)	59	(7.4)
Ureaplasma infection	1	(0.2)	0	(0.0)	1	(0.1)
Urethritis	9	(1.7)	7	(2.6)	16	(2.0)
Urethritis gonococcal	2	(0.4)	2	(0.8)	4	(0.5)
Urinary tract infection	11	(2.1)	3	(1.1)	14	(1.8)
Vaginal infection	1	(0.2)	0	(0.0)	1	(0.1)
Varicella	0	(0.0)	1	(0.4)	1	(0.1)
Vestibular neuronitis	1	(0.2)	0	(0.0)	1	(0.1)
Viral diarrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Viral infection	4	(0.8)	3	(1.1)	7	(0.9)
Viral pharyngitis	2	(0.4)	1	(0.4)	3	(0.4)
Viral skin infection	0	(0.0)	1	(0.4)	1	(0.1)
Viral upper respiratory tract infection	4	(0.8)	1	(0.4)	5	(0.6)
Vulvovaginal candidiasis	5	(0.9)	1	(0.4)	6	(0.8)
Vulvovaginal mycotic infection	1	(0.2)	0	(0.0)	1	(0.1)
Wound infection	1	(0.2)	1	(0.4)	2	(0.3)
Wound infection bacterial	0	(0.0)	1	(0.4)	1	(0.1)
Injury, poisoning and procedural complications	**57**	**(10.7)**	**28**	**(10.5)**	**85**	**(10.7)**
Accidental overdose	22	(4.1)	10	(3.8)	32	(4.0)
Alcohol poisoning	0	(0.0)	1	(0.4)	1	(0.1)
Animal bite	3	(0.6)	0	(0.0)	3	(0.4)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**57**	**(10.7)**	**28**	**(10.5)**	**85**	**(10.7)**
Ankle fracture	1	(0.2)	0	(0.0)	1	(0.1)
Arthropod sting	1	(0.2)	1	(0.4)	2	(0.3)
Burns second degree	0	(0.0)	1	(0.4)	1	(0.1)
Chest injury	1	(0.2)	1	(0.4)	2	(0.3)
Contusion	2	(0.4)	1	(0.4)	3	(0.4)
Epicondylitis	1	(0.2)	0	(0.0)	1	(0.1)
Excoriation	1	(0.2)	0	(0.0)	1	(0.1)
Exposure to communicable disease	1	(0.2)	0	(0.0)	1	(0.1)
Eye injury	0	(0.0)	1	(0.4)	1	(0.1)
Fibula fracture	1	(0.2)	0	(0.0)	1	(0.1)
Foot fracture	0	(0.0)	1	(0.4)	1	(0.1)
Foreign body in eye	0	(0.0)	1	(0.4)	1	(0.1)
Hand fracture	1	(0.2)	0	(0.0)	1	(0.1)
Head injury	4	(0.8)	0	(0.0)	4	(0.5)
Heat stroke	1	(0.2)	0	(0.0)	1	(0.1)
Incision site pain	0	(0.0)	1	(0.4)	1	(0.1)
Intentional overdose	1	(0.2)	0	(0.0)	1	(0.1)
Laceration	2	(0.4)	0	(0.0)	2	(0.3)
Ligament sprain	0	(0.0)	2	(0.8)	2	(0.3)
Limb injury	1	(0.2)	2	(0.8)	3	(0.4)
Lip injury	1	(0.2)	0	(0.0)	1	(0.1)
Muscle strain	2	(0.4)	1	(0.4)	3	(0.4)
Overdose	0	(0.0)	1	(0.4)	1	(0.1)
Post procedural haemorrhage	1	(0.2)	1	(0.4)	2	(0.3)
Procedural pain	1	(0.2)	3	(1.1)	4	(0.5)
Scapula fracture	0	(0.0)	1	(0.4)	1	(0.1)
Seroma	1	(0.2)	0	(0.0)	1	(0.1)
Skin abrasion	2	(0.4)	0	(0.0)	2	(0.3)
Soft tissue injury	0	(0.0)	1	(0.4)	1	(0.1)
Subcutaneous haematoma	2	(0.4)	0	(0.0)	2	(0.3)
Sunburn	1	(0.2)	0	(0.0)	1	(0.1)
Tendon rupture	0	(0.0)	2	(0.8)	2	(0.3)
Thermal burn	3	(0.6)	0	(0.0)	3	(0.4)
Tooth fracture	2	(0.4)	0	(0.0)	2	(0.3)
Toxicity to various agents	1	(0.2)	0	(0.0)	1	(0.1)
Vaccination complication	1	(0.2)	0	(0.0)	1	(0.1)
Wound	2	(0.4)	0	(0.0)	2	(0.3)
Wound secretion	1	(0.2)	0	(0.0)	1	(0.1)
Investigations	**12**	**(2.3)**	**5**	**(1.9)**	**17**	**(2.1)**
Anal pap smear abnormal	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Investigations	**12**	**(2.3)**	**5**	**(1.9)**	**17**	**(2.1)**
Blood pressure decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood pressure increased	5	(0.9)	0	(0.0)	5	(0.6)
Heart rate decreased	1	(0.2)	0	(0.0)	1	(0.1)
Heart rate irregular	1	(0.2)	0	(0.0)	1	(0.1)
Weight decreased	1	(0.2)	2	(0.8)	3	(0.4)
Weight increased	2	(0.4)	3	(1.1)	5	(0.6)
Metabolism and nutrition disorders	**27**	**(5.1)**	**13**	**(4.9)**	**40**	**(5.0)**
Decreased appetite	14	(2.6)	0	(0.0)	14	(1.8)
Dehydration	0	(0.0)	1	(0.4)	1	(0.1)
Diabetes mellitus inadequate control	0	(0.0)	1	(0.4)	1	(0.1)
Gout	0	(0.0)	1	(0.4)	1	(0.1)
Hyperglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hyperproteinaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypertriglyceridaemia	1	(0.2)	2	(0.8)	3	(0.4)
Hypoglycaemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypokalaemia	0	(0.0)	1	(0.4)	1	(0.1)
Hypophosphataemia	1	(0.2)	0	(0.0)	1	(0.1)
Hypovolaemia	1	(0.2)	0	(0.0)	1	(0.1)
Increased appetite	3	(0.6)	1	(0.4)	4	(0.5)
Mineral deficiency	1	(0.2)	0	(0.0)	1	(0.1)
Obesity	1	(0.2)	0	(0.0)	1	(0.1)
Type 2 diabetes mellitus	0	(0.0)	1	(0.4)	1	(0.1)
Vitamin D deficiency	4	(0.8)	5	(1.9)	9	(1.1)
Musculoskeletal and connective tissue disorders	**89**	**(16.8)**	**36**	**(13.5)**	**125**	**(15.7)**
Arthralgia	16	(3.0)	6	(2.3)	22	(2.8)
Back pain	24	(4.5)	8	(3.0)	32	(4.0)
Bone pain	0	(0.0)	1	(0.4)	1	(0.1)
Bursitis	0	(0.0)	1	(0.4)	1	(0.1)
Coccydynia	0	(0.0)	1	(0.4)	1	(0.1)
Costochondritis	3	(0.6)	0	(0.0)	3	(0.4)
Flank pain	3	(0.6)	0	(0.0)	3	(0.4)
Groin pain	0	(0.0)	1	(0.4)	1	(0.1)
Intervertebral disc protrusion	0	(0.0)	1	(0.4)	1	(0.1)
Joint effusion	1	(0.2)	0	(0.0)	1	(0.1)
Joint range of motion decreased	1	(0.2)	0	(0.0)	1	(0.1)
Joint swelling	0	(0.0)	1	(0.4)	1	(0.1)
Monarthritis	1	(0.2)	0	(0.0)	1	(0.1)
Muscle contracture	2	(0.4)	0	(0.0)	2	(0.3)
Muscle spasms	1	(0.2)	2	(0.8)	3	(0.4)

Subjects With Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**89**	**(16.8)**	**36**	**(13.5)**	**125**	**(15.7)**
Muscle tightness	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal chest pain	1	(0.2)	1	(0.4)	2	(0.3)
Musculoskeletal pain	7	(1.3)	5	(1.9)	12	(1.5)
Myalgia	19	(3.6)	7	(2.6)	26	(3.3)
Neck pain	7	(1.3)	2	(0.8)	9	(1.1)
Osteoarthritis	2	(0.4)	0	(0.0)	2	(0.3)
Osteoarthropathy	1	(0.2)	0	(0.0)	1	(0.1)
Pain in extremity	11	(2.1)	4	(1.5)	15	(1.9)
Pain in jaw	1	(0.2)	0	(0.0)	1	(0.1)
Rotator cuff syndrome	3	(0.6)	0	(0.0)	3	(0.4)
Spinal pain	1	(0.2)	0	(0.0)	1	(0.1)
Spondylolisthesis	1	(0.2)	0	(0.0)	1	(0.1)
Synovial cyst	1	(0.2)	0	(0.0)	1	(0.1)
Temporomandibular joint syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Tendonitis	2	(0.4)	3	(1.1)	5	(0.6)
Torticollis	0	(0.0)	1	(0.4)	1	(0.1)
Trismus	1	(0.2)	0	(0.0)	1	(0.1)
Vertebral column mass	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**25**	**(4.7)**	**10**	**(3.8)**	**35**	**(4.4)**
Acrochordon	0	(0.0)	1	(0.4)	1	(0.1)
Anogenital warts	16	(3.0)	2	(0.8)	18	(2.3)
Benign neoplasm of scrotum	1	(0.2)	0	(0.0)	1	(0.1)
Breast cancer in situ	0	(0.0)	1	(0.4)	1	(0.1)
Burkitt's lymphoma	0	(0.0)	1	(0.4)	1	(0.1)
Immunoblastic lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Keratoacanthoma	0	(0.0)	1	(0.4)	1	(0.1)
Lipoma	1	(0.2)	0	(0.0)	1	(0.1)
Melanocytic naevus	0	(0.0)	1	(0.4)	1	(0.1)
Monoclonal gammopathy	1	(0.2)	0	(0.0)	1	(0.1)
Papilloma	1	(0.2)	0	(0.0)	1	(0.1)
Penile wart	1	(0.2)	1	(0.4)	2	(0.3)
Queyrat erythroplasia	0	(0.0)	1	(0.4)	1	(0.1)
Skin papilloma	3	(0.6)	0	(0.0)	3	(0.4)
Thyroid neoplasm	1	(0.2)	0	(0.0)	1	(0.1)
Uterine leiomyoma	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**122**	**(23.0)**	**54**	**(20.3)**	**176**	**(22.1)**
Amnesia	2	(0.4)	1	(0.4)	3	(0.4)
Balance disorder	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**122**	**(23.0)**	**54**	**(20.3)**	**176**	**(22.1)**
Carpal tunnel syndrome	1	(0.2)	1	(0.4)	2	(0.3)
Cognitive disorder	1	(0.2)	0	(0.0)	1	(0.1)
Disturbance in attention	2	(0.4)	0	(0.0)	2	(0.3)
Dizziness	24	(4.5)	12	(4.5)	36	(4.5)
Dysaesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Dysgeusia	1	(0.2)	1	(0.4)	2	(0.3)
Facial paresis	1	(0.2)	0	(0.0)	1	(0.1)
Headache	71	(13.4)	29	(10.9)	100	(12.5)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	2	(0.4)	5	(1.9)	7	(0.9)
Hypotonia	0	(0.0)	1	(0.4)	1	(0.1)
Lethargy	3	(0.6)	2	(0.8)	5	(0.6)
Memory impairment	2	(0.4)	0	(0.0)	2	(0.3)
Migraine	2	(0.4)	1	(0.4)	3	(0.4)
Nerve compression	1	(0.2)	0	(0.0)	1	(0.1)
Neuropathy peripheral	4	(0.8)	0	(0.0)	4	(0.5)
Paraesthesia	4	(0.8)	2	(0.8)	6	(0.8)
Poor quality sleep	1	(0.2)	0	(0.0)	1	(0.1)
Post herpetic neuralgia	3	(0.6)	0	(0.0)	3	(0.4)
Presyncope	1	(0.2)	0	(0.0)	1	(0.1)
Restless legs syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Sciatica	2	(0.4)	0	(0.0)	2	(0.3)
Seizure	2	(0.4)	0	(0.0)	2	(0.3)
Sinus headache	1	(0.2)	0	(0.0)	1	(0.1)
Somnolence	10	(1.9)	2	(0.8)	12	(1.5)
Syncope	4	(0.8)	3	(1.1)	7	(0.9)
Tension headache	0	(0.0)	1	(0.4)	1	(0.1)
Transient ischaemic attack	1	(0.2)	0	(0.0)	1	(0.1)
Vascular headache	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**71**	**(13.4)**	**43**	**(16.2)**	**114**	**(14.3)**
Abnormal dreams	15	(2.8)	7	(2.6)	22	(2.8)
Adjustment disorder	0	(0.0)	1	(0.4)	1	(0.1)
Adjustment disorder with depressed mood	1	(0.2)	0	(0.0)	1	(0.1)
Affective disorder	1	(0.2)	1	(0.4)	2	(0.3)
Agitation	1	(0.2)	0	(0.0)	1	(0.1)
Alcoholism	1	(0.2)	1	(0.4)	2	(0.3)
Anxiety	11	(2.1)	4	(1.5)	15	(1.9)
Anxiety disorder	1	(0.2)	0	(0.0)	1	(0.1)
Attention deficit/hyperactivity disorder	0	(0.0)	1	(0.4)	1	(0.1)
Bipolar disorder	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**71**	**(13.4)**	**43**	**(16.2)**	**114**	**(14.3)**
Borderline personality disorder	1	(0.2)	0	(0.0)	1	(0.1)
Burnout syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Confusional state	1	(0.2)	0	(0.0)	1	(0.1)
Depressed mood	2	(0.4)	0	(0.0)	2	(0.3)
Depression	14	(2.6)	11	(4.1)	25	(3.1)
Distractibility	1	(0.2)	0	(0.0)	1	(0.1)
Drug abuse	2	(0.4)	0	(0.0)	2	(0.3)
Dysthymic disorder	0	(0.0)	1	(0.4)	1	(0.1)
Hallucination	0	(0.0)	1	(0.4)	1	(0.1)
Initial insomnia	0	(0.0)	1	(0.4)	1	(0.1)
Insomnia	21	(4.0)	13	(4.9)	34	(4.3)
Irritability	1	(0.2)	3	(1.1)	4	(0.5)
Libido decreased	4	(0.8)	1	(0.4)	5	(0.6)
Libido disorder	1	(0.2)	0	(0.0)	1	(0.1)
Loss of libido	1	(0.2)	0	(0.0)	1	(0.1)
Major depression	2	(0.4)	0	(0.0)	2	(0.3)
Mental status changes	0	(0.0)	1	(0.4)	1	(0.1)
Middle insomnia	0	(0.0)	1	(0.4)	1	(0.1)
Mood altered	1	(0.2)	0	(0.0)	1	(0.1)
Mood swings	2	(0.4)	1	(0.4)	3	(0.4)
Nervousness	0	(0.0)	1	(0.4)	1	(0.1)
Nightmare	2	(0.4)	1	(0.4)	3	(0.4)
Obsessive-compulsive disorder	0	(0.0)	1	(0.4)	1	(0.1)
Panic attack	0	(0.0)	1	(0.4)	1	(0.1)
Premature ejaculation	1	(0.2)	0	(0.0)	1	(0.1)
Schizophrenia	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	5	(0.9)	2	(0.8)	7	(0.9)
Sleep terror	1	(0.2)	0	(0.0)	1	(0.1)
Stress	0	(0.0)	2	(0.8)	2	(0.3)
Substance abuse	1	(0.2)	0	(0.0)	1	(0.1)
Suicidal ideation	2	(0.4)	1	(0.4)	3	(0.4)
Suicide attempt	1	(0.2)	0	(0.0)	1	(0.1)
Tobacco abuse	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**13**	**(2.4)**	**6**	**(2.3)**	**19**	**(2.4)**
Acute kidney injury	0	(0.0)	1	(0.4)	1	(0.1)
Calculus urinary	1	(0.2)	1	(0.4)	2	(0.3)
Dysuria	5	(0.9)	1	(0.4)	6	(0.8)
IgA nephropathy	1	(0.2)	0	(0.0)	1	(0.1)
Microalbuminuria	1	(0.2)	0	(0.0)	1	(0.1)
Nocturia	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**13**	**(2.4)**	**6**	**(2.3)**	**19**	**(2.4)**
Pollakiuria	1	(0.2)	1	(0.4)	2	(0.3)
Polyuria	1	(0.2)	0	(0.0)	1	(0.1)
Proteinuria	1	(0.2)	0	(0.0)	1	(0.1)
Renal failure	2	(0.4)	2	(0.8)	4	(0.5)
Urinary retention	3	(0.6)	0	(0.0)	3	(0.4)
Reproductive system and breast disorders	**35**	**(6.6)**	**9**	**(3.4)**	**44**	**(5.5)**
Acquired phimosis	1	(0.2)	0	(0.0)	1	(0.1)
Benign prostatic hyperplasia	1	(0.2)	2	(0.8)	3	(0.4)
Breast pain	1	(0.2)	0	(0.0)	1	(0.1)
Cervical dysplasia	5	(0.9)	1	(0.4)	6	(0.8)
Dysfunctional uterine bleeding	0	(0.0)	1	(0.4)	1	(0.1)
Dysmenorrhoea	1	(0.2)	1	(0.4)	2	(0.3)
Erectile dysfunction	3	(0.6)	1	(0.4)	4	(0.5)
Genital burning sensation	1	(0.2)	0	(0.0)	1	(0.1)
Genital cyst	1	(0.2)	0	(0.0)	1	(0.1)
Genital discomfort	2	(0.4)	0	(0.0)	2	(0.3)
Genital lesion	1	(0.2)	0	(0.0)	1	(0.1)
Genital rash	1	(0.2)	1	(0.4)	2	(0.3)
Haematospermia	1	(0.2)	0	(0.0)	1	(0.1)
Menometrorrhagia	1	(0.2)	0	(0.0)	1	(0.1)
Menorrhagia	1	(0.2)	0	(0.0)	1	(0.1)
Pelvic pain	0	(0.0)	1	(0.4)	1	(0.1)
Penile discharge	1	(0.2)	0	(0.0)	1	(0.1)
Penile erythema	1	(0.2)	0	(0.0)	1	(0.1)
Prostatitis	2	(0.4)	2	(0.8)	4	(0.5)
Pruritus genital	2	(0.4)	0	(0.0)	2	(0.3)
Scrotal pain	1	(0.2)	0	(0.0)	1	(0.1)
Sexual dysfunction	1	(0.2)	0	(0.0)	1	(0.1)
Testicular swelling	1	(0.2)	0	(0.0)	1	(0.1)
Testis discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Vaginal discharge	5	(0.9)	0	(0.0)	5	(0.6)
Vaginal haemorrhage	2	(0.4)	0	(0.0)	2	(0.3)
Varicocele	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**76**	**(14.3)**	**40**	**(15.0)**	**116**	**(14.6)**
Asthma	2	(0.4)	2	(0.8)	4	(0.5)
Bronchial hyperreactivity	2	(0.4)	0	(0.0)	2	(0.3)
Bronchospasm	1	(0.2)	0	(0.0)	1	(0.1)
Catarrh	1	(0.2)	0	(0.0)	1	(0.1)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.4)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**76**	**(14.3)**	**40**	**(15.0)**	**116**	**(14.6)**
Cough	28	(5.3)	14	(5.3)	42	(5.3)
Dysphonia	1	(0.2)	0	(0.0)	1	(0.1)
Dyspnoea	2	(0.4)	1	(0.4)	3	(0.4)
Epistaxis	6	(1.1)	1	(0.4)	7	(0.9)
Hiccups	1	(0.2)	0	(0.0)	1	(0.1)
Nasal congestion	6	(1.1)	6	(2.3)	12	(1.5)
Nasal obstruction	1	(0.2)	0	(0.0)	1	(0.1)
Nasal polyps	1	(0.2)	0	(0.0)	1	(0.1)
Nasal ulcer	0	(0.0)	1	(0.4)	1	(0.1)
Oropharyngeal pain	20	(3.8)	9	(3.4)	29	(3.6)
Paranasal sinus discomfort	2	(0.4)	0	(0.0)	2	(0.3)
Pharyngeal erythema	0	(0.0)	1	(0.4)	1	(0.1)
Pleural effusion	1	(0.2)	0	(0.0)	1	(0.1)
Productive cough	3	(0.6)	1	(0.4)	4	(0.5)
Respiratory disorder	1	(0.2)	1	(0.4)	2	(0.3)
Rhinitis allergic	15	(2.8)	6	(2.3)	21	(2.6)
Rhinorrhoea	8	(1.5)	2	(0.8)	10	(1.3)
Rhonchi	1	(0.2)	0	(0.0)	1	(0.1)
Sinus congestion	5	(0.9)	3	(1.1)	8	(1.0)
Tonsillar ulcer	1	(0.2)	0	(0.0)	1	(0.1)
Upper-airway cough syndrome	1	(0.2)	1	(0.4)	2	(0.3)
Wheezing	1	(0.2)	1	(0.4)	2	(0.3)
Skin and subcutaneous tissue disorders	**101**	**(19.0)**	**63**	**(23.7)**	**164**	**(20.6)**
Acne	10	(1.9)	3	(1.1)	13	(1.6)
Acne cystic	1	(0.2)	0	(0.0)	1	(0.1)
Alopecia	2	(0.4)	0	(0.0)	2	(0.3)
Androgenetic alopecia	0	(0.0)	1	(0.4)	1	(0.1)
Cold sweat	1	(0.2)	0	(0.0)	1	(0.1)
Dermal cyst	2	(0.4)	2	(0.8)	4	(0.5)
Dermatitis	5	(0.9)	3	(1.1)	8	(1.0)
Dermatitis allergic	4	(0.8)	0	(0.0)	4	(0.5)
Dermatitis contact	2	(0.4)	1	(0.4)	3	(0.4)
Drug eruption	0	(0.0)	2	(0.8)	2	(0.3)
Dry skin	6	(1.1)	3	(1.1)	9	(1.1)
Dyshidrotic eczema	0	(0.0)	2	(0.8)	2	(0.3)
Ecchymosis	1	(0.2)	1	(0.4)	2	(0.3)
Eczema	7	(1.3)	2	(0.8)	9	(1.1)
Eczema nummular	0	(0.0)	1	(0.4)	1	(0.1)
Eosinophilic pustular folliculitis	1	(0.2)	0	(0.0)	1	(0.1)
Erythema	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**101**	**(19.0)**	**63**	**(23.7)**	**164**	**(20.6)**
Hand dermatitis	0	(0.0)	1	(0.4)	1	(0.1)
Hyperhidrosis	4	(0.8)	1	(0.4)	5	(0.6)
Hyperkeratosis	0	(0.0)	1	(0.4)	1	(0.1)
Intertrigo	1	(0.2)	1	(0.4)	2	(0.3)
Lipodystrophy acquired	1	(0.2)	2	(0.8)	3	(0.4)
Macule	0	(0.0)	1	(0.4)	1	(0.1)
Miliaria	1	(0.2)	0	(0.0)	1	(0.1)
Neurodermatitis	0	(0.0)	1	(0.4)	1	(0.1)
Night sweats	1	(0.2)	3	(1.1)	4	(0.5)
Palmoplantar keratoderma	1	(0.2)	0	(0.0)	1	(0.1)
Papule	3	(0.6)	1	(0.4)	4	(0.5)
Peau d'orange	1	(0.2)	0	(0.0)	1	(0.1)
Photosensitivity reaction	1	(0.2)	0	(0.0)	1	(0.1)
Pityriasis rosea	1	(0.2)	0	(0.0)	1	(0.1)
Post inflammatory pigmentation change	0	(0.0)	1	(0.4)	1	(0.1)
Pruritus	15	(2.8)	15	(5.6)	30	(3.8)
Pruritus generalised	1	(0.2)	1	(0.4)	2	(0.3)
Pseudofolliculitis barbae	1	(0.2)	0	(0.0)	1	(0.1)
Psoriasis	1	(0.2)	0	(0.0)	1	(0.1)
Rash	23	(4.3)	11	(4.1)	34	(4.3)
Rash generalised	0	(0.0)	1	(0.4)	1	(0.1)
Rash maculo-papular	2	(0.4)	0	(0.0)	2	(0.3)
Rash papular	8	(1.5)	4	(1.5)	12	(1.5)
Rash pruritic	1	(0.2)	2	(0.8)	3	(0.4)
Rosacea	1	(0.2)	0	(0.0)	1	(0.1)
Scab	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoea	1	(0.2)	0	(0.0)	1	(0.1)
Seborrhoeic dermatitis	5	(0.9)	3	(1.1)	8	(1.0)
Skin exfoliation	1	(0.2)	0	(0.0)	1	(0.1)
Skin hyperpigmentation	0	(0.0)	1	(0.4)	1	(0.1)
Skin lesion	2	(0.4)	3	(1.1)	5	(0.6)
Skin maceration	0	(0.0)	1	(0.4)	1	(0.1)
Skin mass	1	(0.2)	0	(0.0)	1	(0.1)
Skin plaque	1	(0.2)	0	(0.0)	1	(0.1)
Skin ulcer	2	(0.4)	0	(0.0)	2	(0.3)
Swelling face	1	(0.2)	0	(0.0)	1	(0.1)
Telangiectasia	1	(0.2)	0	(0.0)	1	(0.1)
Urticaria	1	(0.2)	2	(0.8)	3	(0.4)
Vitiligo	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**25**	**(4.7)**	**11**	**(4.1)**	**36**	**(4.5)**

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**25**	**(4.7)**	**11**	**(4.1)**	**36**	**(4.5)**
Deep vein thrombosis	1	(0.2)	0	(0.0)	1	(0.1)
Haematoma	1	(0.2)	0	(0.0)	1	(0.1)
Hot flush	3	(0.6)	1	(0.4)	4	(0.5)
Hypertension	16	(3.0)	7	(2.6)	23	(2.9)
Hypertensive crisis	1	(0.2)	0	(0.0)	1	(0.1)
Hypotension	1	(0.2)	0	(0.0)	1	(0.1)
Peripheral coldness	1	(0.2)	0	(0.0)	1	(0.1)
Phlebitis	1	(0.2)	0	(0.0)	1	(0.1)
Systolic hypertension	0	(0.0)	1	(0.4)	1	(0.1)
Varicose vein	0	(0.0)	1	(0.4)	1	(0.1)
Vasodilatation	0	(0.0)	1	(0.4)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 8

Subjects With Drug-Related Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class - Overall Drug Related
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more drug-related adverse events	130	(24.5)	68	(25.6)	198	(24.8)
with no drug-related adverse events	401	(75.5)	198	(74.4)	599	(75.2)
Blood and lymphatic system disorders	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
Anaemia	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	0	(0.0)	1	(0.4)	1	(0.1)
Cardiac disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
Palpitations	1	(0.2)	0	(0.0)	1	(0.1)
Tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
Conjunctival haemorrhage	0	(0.0)	1	(0.4)	1	(0.1)
Eye irritation	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**76**	**(14.3)**	**32**	**(12.0)**	**108**	**(13.6)**
Abdominal discomfort	2	(0.4)	2	(0.8)	4	(0.5)
Abdominal distension	5	(0.9)	4	(1.5)	9	(1.1)
Abdominal pain	16	(3.0)	2	(0.8)	18	(2.3)
Abdominal pain upper	4	(0.8)	1	(0.4)	5	(0.6)
Abnormal faeces	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	12	(2.3)	7	(2.6)	19	(2.4)
Dry mouth	2	(0.4)	1	(0.4)	3	(0.4)
Dyspepsia	4	(0.8)	0	(0.0)	4	(0.5)
Epigastric discomfort	1	(0.2)	0	(0.0)	1	(0.1)
Faeces soft	0	(0.0)	1	(0.4)	1	(0.1)
Flatulence	3	(0.6)	5	(1.9)	8	(1.0)
Frequent bowel movements	1	(0.2)	1	(0.4)	2	(0.3)
Gastrooesophageal reflux disease	2	(0.4)	0	(0.0)	2	(0.3)
Hypoaesthesia oral	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	0	(0.0)	1	(0.4)	1	(0.1)
Nausea	39	(7.3)	18	(6.8)	57	(7.2)
Odynophagia	0	(0.0)	1	(0.4)	1	(0.1)
Vomiting	13	(2.4)	3	(1.1)	16	(2.0)
General disorders and administration site conditions	**15**	**(2.8)**	**8**	**(3.0)**	**23**	**(2.9)**
Asthenia	2	(0.4)	2	(0.8)	4	(0.5)
Drug ineffective	0	(0.0)	1	(0.4)	1	(0.1)
Drug withdrawal syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Fatigue	9	(1.7)	2	(0.8)	11	(1.4)

Subjects With Drug-Related Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**15**	**(2.8)**	**8**	**(3.0)**	**23**	**(2.9)**
Feeling abnormal	0	(0.0)	1	(0.4)	1	(0.1)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Hunger	0	(0.0)	1	(0.4)	1	(0.1)
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Sluggishness	0	(0.0)	1	(0.4)	1	(0.1)
Thirst	1	(0.2)	1	(0.4)	2	(0.3)
Infections and infestations	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.5)**
Anal abscess	1	(0.2)	0	(0.0)	1	(0.1)
Angular cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chikungunya virus infection	1	(0.2)	0	(0.0)	1	(0.1)
Epididymitis	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**14**	**(2.6)**	**1**	**(0.4)**	**15**	**(1.9)**
Decreased appetite	11	(2.1)	0	(0.0)	11	(1.4)
Hypophosphataemia	1	(0.2)	0	(0.0)	1	(0.1)
Increased appetite	2	(0.4)	1	(0.4)	3	(0.4)
Musculoskeletal and connective tissue disorders	**4**	**(0.8)**	**5**	**(1.9)**	**9**	**(1.1)**
Arthralgia	1	(0.2)	0	(0.0)	1	(0.1)
Back pain	0	(0.0)	1	(0.4)	1	(0.1)
Bone pain	0	(0.0)	1	(0.4)	1	(0.1)
Myalgia	3	(0.6)	1	(0.4)	4	(0.5)
Pain in extremity	0	(0.0)	1	(0.4)	1	(0.1)
Tendonitis	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**38**	**(7.2)**	**23**	**(8.6)**	**61**	**(7.7)**
Dizziness	12	(2.3)	8	(3.0)	20	(2.5)
Dysgeusia	1	(0.2)	1	(0.4)	2	(0.3)
Headache	16	(3.0)	12	(4.5)	28	(3.5)
Hypersomnia	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	0	(0.0)	1	(0.4)	1	(0.1)
Lethargy	3	(0.6)	1	(0.4)	4	(0.5)
Memory impairment	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	1	(0.2)	0	(0.0)	1	(0.1)
Post herpetic neuralgia	1	(0.2)	0	(0.0)	1	(0.1)
Seizure	2	(0.4)	0	(0.0)	2	(0.3)
Somnolence	5	(0.9)	1	(0.4)	6	(0.8)
Syncope	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**20**	**(3.8)**	**10**	**(3.8)**	**30**	**(3.8)**
Abnormal dreams	9	(1.7)	4	(1.5)	13	(1.6)
Affective disorder	0	(0.0)	1	(0.4)	1	(0.1)
Agitation	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	1	(0.2)	0	(0.0)	1	(0.1)
Insomnia	8	(1.5)	3	(1.1)	11	(1.4)
Libido decreased	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	0	(0.0)	1	(0.4)	1	(0.1)
Mood swings	1	(0.2)	0	(0.0)	1	(0.1)
Nightmare	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	1	(0.2)	2	(0.8)	3	(0.4)
Renal and urinary disorders	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
Renal failure	1	(0.2)	2	(0.8)	3	(0.4)
Reproductive system and breast disorders	**3**	**(0.6)**	**1**	**(0.4)**	**4**	**(0.5)**
Erectile dysfunction	2	(0.4)	1	(0.4)	3	(0.4)
Haematospermia	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Sinus congestion	0	(0.0)	1	(0.4)	1	(0.1)
Skin and subcutaneous tissue disorders	**16**	**(3.0)**	**9**	**(3.4)**	**25**	**(3.1)**
Acne	1	(0.2)	0	(0.0)	1	(0.1)
Alopecia	2	(0.4)	0	(0.0)	2	(0.3)
Dermatitis allergic	2	(0.4)	0	(0.0)	2	(0.3)
Drug eruption	0	(0.0)	1	(0.4)	1	(0.1)
Ecchymosis	0	(0.0)	1	(0.4)	1	(0.1)
Hyperhidrosis	1	(0.2)	1	(0.4)	2	(0.3)
Lipodystrophy acquired	0	(0.0)	1	(0.4)	1	(0.1)
Pityriasis rosea	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	2	(0.4)	1	(0.4)	3	(0.4)
Pruritus generalised	1	(0.2)	1	(0.4)	2	(0.3)
Rash	4	(0.8)	1	(0.4)	5	(0.6)
Rash generalised	0	(0.0)	1	(0.4)	1	(0.1)
Rash papular	4	(0.8)	1	(0.4)	5	(0.6)
Skin hyperpigmentation	0	(0.0)	1	(0.4)	1	(0.1)
Vascular disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**

Subjects With Drug-Related Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
Hot flush	2	(0.4)	0	(0.0)	2	(0.3)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 9

Subjects With Drug-Related Clinical Adverse Events (Incidence ≥ 2% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more drug-related adverse events	130	(24.5)	68	(25.6)	198	(24.8)
with no drug-related adverse events	401	(75.5)	198	(74.4)	599	(75.2)
Gastrointestinal disorders	**76**	**(14.3)**	**32**	**(12.0)**	**108**	**(13.6)**
Abdominal pain	16	(3.0)	2	(0.8)	18	(2.3)
Diarrhoea	12	(2.3)	7	(2.6)	19	(2.4)
Nausea	39	(7.3)	18	(6.8)	57	(7.2)
Vomiting	13	(2.4)	3	(1.1)	16	(2.0)
General disorders and administration site conditions	**15**	**(2.8)**	**8**	**(3.0)**	**23**	**(2.9)**
Metabolism and nutrition disorders	**14**	**(2.6)**	**1**	**(0.4)**	**15**	**(1.9)**
Decreased appetite	11	(2.1)	0	(0.0)	11	(1.4)
Nervous system disorders	**38**	**(7.2)**	**23**	**(8.6)**	**61**	**(7.7)**
Dizziness	12	(2.3)	8	(3.0)	20	(2.5)
Headache	16	(3.0)	12	(4.5)	28	(3.5)
Psychiatric disorders	**20**	**(3.8)**	**10**	**(3.8)**	**30**	**(3.8)**
Skin and subcutaneous tissue disorders	**16**	**(3.0)**	**9**	**(3.4)**	**25**	**(3.1)**

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 10

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship
(Incidence ≥2% in One or More Treatment Groups)
Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		531		266		797	
With one or more drug-related adverse events	Overall	130	(24.5)	68	(25.6)	198	(24.8)
	Raltegravir	124	(23.4)	66	(24.8)	190	(23.8)
Gastrointestinal disorders	**Overall**	**76**	**(14.3)**	**32**	**(12.0)**	**108**	**(13.6)**
	Raltegravir	71	(13.4)	31	(11.7)	102	(12.8)
Abdominal pain	Overall	16	(3.0)	2	(0.8)	18	(2.3)
	Raltegravir	15	(2.8)	1	(0.4)	16	(2.0)
Diarrhoea	Overall	12	(2.3)	7	(2.6)	19	(2.4)
	Raltegravir	10	(1.9)	7	(2.6)	17	(2.1)
Nausea	Overall	39	(7.3)	18	(6.8)	57	(7.2)
	Raltegravir	36	(6.8)	18	(6.8)	54	(6.8)
Vomiting	Overall	13	(2.4)	3	(1.1)	16	(2.0)
	Raltegravir	13	(2.4)	3	(1.1)	16	(2.0)
General disorders and administration site conditions	**Overall**	**15**	**(2.8)**	**8**	**(3.0)**	**23**	**(2.9)**
	Raltegravir	14	(2.6)	8	(3.0)	22	(2.8)
Metabolism and nutrition disorders	**Overall**	**14**	**(2.6)**	**1**	**(0.4)**	**15**	**(1.9)**
	Raltegravir	14	(2.6)	1	(0.4)	15	(1.9)
Decreased appetite	Overall	11	(2.1)	0	(0.0)	11	(1.4)
	Raltegravir	11	(2.1)	0	(0.0)	11	(1.4)
Nervous system disorders	**Overall**	**38**	**(7.2)**	**23**	**(8.6)**	**61**	**(7.7)**
	Raltegravir	36	(6.8)	23	(8.6)	59	(7.4)
Dizziness	Overall	12	(2.3)	8	(3.0)	20	(2.5)
	Raltegravir	12	(2.3)	8	(3.0)	20	(2.5)
Headache	Overall	16	(3.0)	12	(4.5)	28	(3.5)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence ≥2% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
	Raltegravir	14	(2.6)	12	(4.5)	26	(3.3)
Psychiatric disorders	**Overall**	**20**	**(3.8)**	**10**	**(3.8)**	**30**	**(3.8)**
	Raltegravir	20	(3.8)	10	(3.8)	30	(3.8)
Skin and subcutaneous tissue disorders	**Overall**	**16**	**(3.0)**	**9**	**(3.4)**	**25**	**(3.1)**
	Raltegravir	15	(2.8)	9	(3.4)	24	(3.0)

Every subject is counted once on each applicable row.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.

Relationship: study medication(s) to which the investigator attributed the adverse event. Raltegravir (alone or in combination with TRUVADA™), open label TRUVADA™ only.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 11

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship
(Incidence >0% in One or More Treatment Groups)
Weeks 0-48

		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	Relationship	n	(%)	n	(%)	n	(%)
Subjects in population		531		266		797	
With one or more drug-related adverse events	Overall	130	(24.5)	68	(25.6)	198	(24.8)
	Raltegravir	124	(23.4)	66	(24.8)	190	(23.8)
	TRUVADA™ only	10	(1.9)	5	(1.9)	15	(1.9)
Blood and lymphatic system disorders	**Overall**	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Anaemia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Thrombocytopenia	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Cardiac disorders	**Overall**	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
Palpitations	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Tachycardia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Eye disorders	**Overall**	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Conjunctival haemorrhage	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Eye irritation	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**Overall**	**76**	**(14.3)**	**32**	**(12.0)**	**108**	**(13.6)**
	Raltegravir	71	(13.4)	31	(11.7)	102	(12.8)
	TRUVADA™ only	7	(1.3)	2	(0.8)	9	(1.1)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	Relationship	n	(%)	n	(%)	n	(%)
Abdominal discomfort	Overall	2	(0.4)	2	(0.8)	4	(0.5)
	Raltegravir	2	(0.4)	2	(0.8)	4	(0.5)
Abdominal distension	Overall	5	(0.9)	4	(1.5)	9	(1.1)
	Raltegravir	5	(0.9)	3	(1.1)	8	(1.0)
	TRUVADA™ only	0	(0.0)	1	(0.4)	1	(0.1)
Abdominal pain	Overall	16	(3.0)	2	(0.8)	18	(2.3)
	Raltegravir	15	(2.8)	1	(0.4)	16	(2.0)
	TRUVADA™ only	1	(0.2)	1	(0.4)	2	(0.3)
Abdominal pain upper	Overall	4	(0.8)	1	(0.4)	5	(0.6)
	Raltegravir	4	(0.8)	1	(0.4)	5	(0.6)
Abnormal faeces	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	Overall	12	(2.3)	7	(2.6)	19	(2.4)
	Raltegravir	10	(1.9)	7	(2.6)	17	(2.1)
	TRUVADA™ only	2	(0.4)	0	(0.0)	2	(0.3)
Dry mouth	Overall	2	(0.4)	1	(0.4)	3	(0.4)
	Raltegravir	2	(0.4)	1	(0.4)	3	(0.4)
Dyspepsia	Overall	4	(0.8)	0	(0.0)	4	(0.5)
	Raltegravir	4	(0.8)	0	(0.0)	4	(0.5)
Epigastric discomfort	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Faeces soft	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Flatulence	Overall	3	(0.6)	5	(1.9)	8	(1.0)
	Raltegravir	2	(0.4)	3	(1.1)	5	(0.6)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	Relationship	n	(%)	n	(%)	n	(%)
	TRUVADA™ only	1	(0.2)	2	(0.8)	3	(0.4)
Frequent bowel movements	Overall	1	(0.2)	1	(0.4)	2	(0.3)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Gastrooesophageal reflux disease	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
Hypoaesthesia oral	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Mouth ulceration	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Nausea	Overall	39	(7.3)	18	(6.8)	57	(7.2)
	Raltegravir	36	(6.8)	18	(6.8)	54	(6.8)
	TRUVADA™ only	3	(0.6)	0	(0.0)	3	(0.4)
Odynophagia	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Vomiting	Overall	13	(2.4)	3	(1.1)	16	(2.0)
	Raltegravir	13	(2.4)	3	(1.1)	16	(2.0)
General disorders and administration site conditions	**Overall**	**15**	**(2.8)**	**8**	**(3.0)**	**23**	**(2.9)**
	Raltegravir	14	(2.6)	8	(3.0)	22	(2.8)
	TRUVADA™ only	1	(0.2)	0	(0.0)	1	(0.1)
Asthenia	Overall	2	(0.4)	2	(0.8)	4	(0.5)
	Raltegravir	2	(0.4)	2	(0.8)	4	(0.5)
Drug ineffective	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Drug withdrawal syndrome	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Fatigue	Overall	9	(1.7)	2	(0.8)	11	(1.4)
	Raltegravir	9	(1.7)	2	(0.8)	11	(1.4)
Feeling abnormal	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Feeling hot	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	TRUVADA™ only	1	(0.2)	0	(0.0)	1	(0.1)
Hunger	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Pyrexia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Sluggishness	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Thirst	Overall	1	(0.2)	1	(0.4)	2	(0.3)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Infections and infestations	**Overall**	**4**	**(0.8)**	**0**	**(0.0)**	**4**	**(0.5)**
	Raltegravir	4	(0.8)	0	(0.0)	4	(0.5)
Anal abscess	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Angular cheilitis	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Chikungunya virus infection	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Epididymitis	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**Overall**	**14**	**(2.6)**	**1**	**(0.4)**	**15**	**(1.9)**
	Raltegravir	14	(2.6)	1	(0.4)	15	(1.9)
Decreased appetite	Overall	11	(2.1)	0	(0.0)	11	(1.4)
	Raltegravir	11	(2.1)	0	(0.0)	11	(1.4)
Hypophosphataemia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Increased appetite	Overall	2	(0.4)	1	(0.4)	3	(0.4)
	Raltegravir	2	(0.4)	1	(0.4)	3	(0.4)
Musculoskeletal and connective tissue disorders	**Overall**	**4**	**(0.8)**	**5**	**(1.9)**	**9**	**(1.1)**
	Raltegravir	4	(0.8)	4	(1.5)	8	(1.0)
	TRUVADA™ only	0	(0.0)	1	(0.4)	1	(0.1)
Arthralgia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Back pain	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Bone pain	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	TRUVADA™ only	0	(0.0)	1	(0.4)	1	(0.1)
Myalgia	Overall	3	(0.6)	1	(0.4)	4	(0.5)
	Raltegravir	3	(0.6)	1	(0.4)	4	(0.5)
Pain in extremity	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Tendonitis	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**Overall**	**38**	**(7.2)**	**23**	**(8.6)**	**61**	**(7.7)**

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	Relationship	n	(%)	n	(%)	n	(%)
	Raltegravir	36	(6.8)	23	(8.6)	59	(7.4)
	TRUVADA™ only	2	(0.4)	0	(0.0)	2	(0.3)
Dizziness	Overall	12	(2.3)	8	(3.0)	20	(2.5)
	Raltegravir	12	(2.3)	8	(3.0)	20	(2.5)
Dysgeusia	Overall	1	(0.2)	1	(0.4)	2	(0.3)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Headache	Overall	16	(3.0)	12	(4.5)	28	(3.5)
	Raltegravir	14	(2.6)	12	(4.5)	26	(3.3)
	TRUVADA™ only	2	(0.4)	0	(0.0)	2	(0.3)
Hypersomnia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Hypoaesthesia	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Lethargy	Overall	3	(0.6)	1	(0.4)	4	(0.5)
	Raltegravir	3	(0.6)	1	(0.4)	4	(0.5)
Memory impairment	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Paraesthesia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Post herpetic neuralgia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Seizure	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
Somnolence	Overall	5	(0.9)	1	(0.4)	6	(0.8)
	Raltegravir	5	(0.9)	1	(0.4)	6	(0.8)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Syncope	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**Overall**	**20**	**(3.8)**	**10**	**(3.8)**	**30**	**(3.8)**
	Raltegravir	20	(3.8)	10	(3.8)	30	(3.8)
Abnormal dreams	Overall	9	(1.7)	4	(1.5)	13	(1.6)
	Raltegravir	9	(1.7)	4	(1.5)	13	(1.6)
Affective disorder	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Agitation	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Anxiety	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Insomnia	Overall	8	(1.5)	3	(1.1)	11	(1.4)
	Raltegravir	8	(1.5)	3	(1.1)	11	(1.4)
Libido decreased	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Middle insomnia	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Mood swings	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Nightmare	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Sleep disorder	Overall	1	(0.2)	2	(0.8)	3	(0.4)
	Raltegravir	1	(0.2)	2	(0.8)	3	(0.4)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**Overall**	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
	TRUVADA™ only	0	(0.0)	2	(0.8)	2	(0.3)
Renal failure	Overall	1	(0.2)	2	(0.8)	3	(0.4)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
	TRUVADA™ only	0	(0.0)	2	(0.8)	2	(0.3)
Reproductive system and breast disorders	**Overall**	**3**	**(0.6)**	**1**	**(0.4)**	**4**	**(0.5)**
	Raltegravir	3	(0.6)	1	(0.4)	4	(0.5)
Erectile dysfunction	Overall	2	(0.4)	1	(0.4)	3	(0.4)
	Raltegravir	2	(0.4)	1	(0.4)	3	(0.4)
Haematospermia	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**Overall**	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Sinus congestion	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Skin and subcutaneous tissue disorders	**Overall**	**16**	**(3.0)**	**9**	**(3.4)**	**25**	**(3.1)**
	Raltegravir	15	(2.8)	9	(3.4)	24	(3.0)
	TRUVADA™ only	1	(0.2)	0	(0.0)	1	(0.1)
Acne	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Alopecia	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
Dermatitis allergic	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Drug eruption	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Ecchymosis	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Hyperhidrosis	Overall	1	(0.2)	1	(0.4)	2	(0.3)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Lipodystrophy acquired	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Pityriasis rosea	Overall	1	(0.2)	0	(0.0)	1	(0.1)
	Raltegravir	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus	Overall	2	(0.4)	1	(0.4)	3	(0.4)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
	TRUVADA™ only	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus generalised	Overall	1	(0.2)	1	(0.4)	2	(0.3)
	Raltegravir	1	(0.2)	1	(0.4)	2	(0.3)
Rash	Overall	4	(0.8)	1	(0.4)	5	(0.6)
	Raltegravir	4	(0.8)	1	(0.4)	5	(0.6)
Rash generalised	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Rash papular	Overall	4	(0.8)	1	(0.4)	5	(0.6)
	Raltegravir	4	(0.8)	1	(0.4)	5	(0.6)
Skin hyperpigmentation	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)
Vascular disorders	**Overall**	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**

Subjects With Drug-Related Clinical Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

		Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	Relationship	n	(%)	n	(%)	n	(%)
Hot flush	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)

Every subject is counted once on each applicable row.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.

Relationship: study medication(s) to which the investigator attributed the adverse event. Raltegravir (alone or in combination with TRUVADA™), open label TRUVADA™ only.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 12

Subjects With Drug-Related Clinical Adverse Events of Moderate or Severe Intensities
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class - Overall Drug Related
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more drug-related adverse events	31	(5.8)	13	(4.9)	44	(5.5)
with no drug-related adverse events	500	(94.2)	253	(95.1)	753	(94.5)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Thrombocytopenia	0	(0.0)	1	(0.4)	1	(0.1)
Cardiac disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Tachycardia	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**12**	**(2.3)**	**4**	**(1.5)**	**16**	**(2.0)**
Abdominal discomfort	1	(0.2)	1	(0.4)	2	(0.3)
Abdominal distension	2	(0.4)	1	(0.4)	3	(0.4)
Abdominal pain	3	(0.6)	1	(0.4)	4	(0.5)
Abdominal pain upper	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea	1	(0.2)	1	(0.4)	2	(0.3)
Flatulence	0	(0.0)	2	(0.8)	2	(0.3)
Nausea	7	(1.3)	0	(0.0)	7	(0.9)
Vomiting	4	(0.8)	0	(0.0)	4	(0.5)
General disorders and administration site conditions	**3**	**(0.6)**	**1**	**(0.4)**	**4**	**(0.5)**
Asthenia	1	(0.2)	0	(0.0)	1	(0.1)
Drug ineffective	0	(0.0)	1	(0.4)	1	(0.1)
Drug withdrawal syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Feeling hot	1	(0.2)	0	(0.0)	1	(0.1)
Thirst	0	(0.0)	1	(0.4)	1	(0.1)
Infections and infestations	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
Angular cheilitis	1	(0.2)	0	(0.0)	1	(0.1)
Chikungunya virus infection	1	(0.2)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.1)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Back pain	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**10**	**(1.9)**	**1**	**(0.4)**	**11**	**(1.4)**
Dizziness	2	(0.4)	0	(0.0)	2	(0.3)
Headache	5	(0.9)	1	(0.4)	6	(0.8)

Subjects With Drug-Related Clinical Adverse Events of Moderate or Severe Intensities (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Nervous system disorders	**10**	**(1.9)**	**1**	**(0.4)**	**11**	**(1.4)**
Memory impairment	1	(0.2)	0	(0.0)	1	(0.1)
Seizure	2	(0.4)	0	(0.0)	2	(0.3)
Syncope	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**3**	**(0.6)**	**3**	**(1.1)**	**6**	**(0.8)**
Affective disorder	0	(0.0)	1	(0.4)	1	(0.1)
Anxiety	1	(0.2)	0	(0.0)	1	(0.1)
Insomnia	2	(0.4)	1	(0.4)	3	(0.4)
Sleep disorder	0	(0.0)	1	(0.4)	1	(0.1)
Renal and urinary disorders	**0**	**(0.0)**	**2**	**(0.8)**	**2**	**(0.3)**
Renal failure	0	(0.0)	2	(0.8)	2	(0.3)
Reproductive system and breast disorders	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
Erectile dysfunction	1	(0.2)	1	(0.4)	2	(0.3)
Skin and subcutaneous tissue disorders	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**
Drug eruption	0	(0.0)	1	(0.4)	1	(0.1)
Hyperhidrosis	0	(0.0)	1	(0.4)	1	(0.1)
Pityriasis rosea	1	(0.2)	0	(0.0)	1	(0.1)
Pruritus generalised	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 13

Subjects With Drug-Related Clinical Adverse Events of Moderate or Severe Intensities
(Incidence ≥ 2% in One or More Treatment Groups)
by System Organ Class - Overall Drug Related
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more drug-related adverse events	31	(5.8)	13	(4.9)	44	(5.5)
with no drug-related adverse events	500	(94.2)	253	(95.1)	753	(94.5)
Gastrointestinal disorders	**12**	**(2.3)**	**4**	**(1.5)**	**16**	**(2.0)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 14

Subjects With Serious Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n	(%)	n	(%)
Subjects in population	531		266	
with one or more serious adverse events	31	(5.8)	25	(9.4)
with no serious adverse events	500	(94.2)	241	(90.6)
Cardiac disorders	**1**	**(0.2)**	**0**	**(0.0)**
Acute coronary syndrome	1	(0.2)	0	(0.0)
Gastrointestinal disorders	**3**	**(0.6)**	**3**	**(1.1)**
Gastritis	0	(0.0)	2	(0.8)
Gastrointestinal perforation	1	(0.2)	0	(0.0)
Proctitis	2	(0.4)	0	(0.0)
Vomiting	0	(0.0)	1	(0.4)
General disorders and administration site conditions	**1**	**(0.2)**	**1**	**(0.4)**
Drug ineffective	0	(0.0)	1	(0.4)
Peripheral swelling	1	(0.2)	0	(0.0)
Hepatobiliary disorders	**2**	**(0.4)**	**0**	**(0.0)**
Cholecystitis	1	(0.2)	0	(0.0)
Hepatitis acute	1	(0.2)	0	(0.0)
Infections and infestations	**13**	**(2.4)**	**11**	**(4.1)**
Abdominal wall abscess	1	(0.2)	0	(0.0)
Acquired immunodeficiency syndrome	0	(0.0)	1	(0.4)
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)
Dengue fever	1	(0.2)	0	(0.0)
Diarrhoea infectious	1	(0.2)	0	(0.0)
Gastroenteritis	2	(0.4)	1	(0.4)
Gastroenteritis bacterial	0	(0.0)	1	(0.4)
Gastroenteritis norovirus	1	(0.2)	0	(0.0)
Hepatitis C	1	(0.2)	0	(0.0)
Lymphogranuloma venereum	0	(0.0)	1	(0.4)
Osteomyelitis	0	(0.0)	1	(0.4)
Otitis externa	0	(0.0)	1	(0.4)
Perineal abscess	0	(0.0)	1	(0.4)
Pharyngitis	1	(0.2)	0	(0.0)
Pneumonia	1	(0.2)	0	(0.0)
Proctitis chlamydial	1	(0.2)	0	(0.0)
Subcutaneous abscess	0	(0.0)	1	(0.4)
Syphilis	1	(0.2)	0	(0.0)
Tuberculosis	1	(0.2)	1	(0.4)
Varicella	0	(0.0)	1	(0.4)
Vestibular neuronitis	1	(0.2)	0	(0.0)

Subjects With Serious Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n	(%)	n	(%)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**3**	**(1.1)**
Alcohol poisoning	0	(0.0)	1	(0.4)
Foot fracture	0	(0.0)	1	(0.4)
Head injury	1	(0.2)	0	(0.0)
Post procedural haemorrhage	1	(0.2)	0	(0.0)
Tendon rupture	0	(0.0)	1	(0.4)
Musculoskeletal and connective tissue disorders	**1**	**(0.2)**	**0**	**(0.0)**
Back pain	1	(0.2)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.4)**	**3**	**(1.1)**
Anogenital warts	1	(0.2)	0	(0.0)
Breast cancer in situ	0	(0.0)	1	(0.4)
Burkitt's lymphoma	0	(0.0)	1	(0.4)
Immunoblastic lymphoma	1	(0.2)	0	(0.0)
Queyrat erythroplasia	0	(0.0)	1	(0.4)
Nervous system disorders	**3**	**(0.6)**	**0**	**(0.0)**
Facial paresis	1	(0.2)	0	(0.0)
Headache	1	(0.2)	0	(0.0)
Transient ischaemic attack	1	(0.2)	0	(0.0)
Psychiatric disorders	**4**	**(0.8)**	**1**	**(0.4)**
Alcoholism	1	(0.2)	1	(0.4)
Depression	3	(0.6)	1	(0.4)
Schizophrenia	1	(0.2)	0	(0.0)
Suicide attempt	1	(0.2)	0	(0.0)
Renal and urinary disorders	**2**	**(0.4)**	**2**	**(0.8)**
Acute kidney injury	0	(0.0)	1	(0.4)
Calculus urinary	1	(0.2)	1	(0.4)
Renal failure	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	**0**	**(0.0)**	**2**	**(0.8)**
Benign prostatic hyperplasia	0	(0.0)	1	(0.4)
Prostatitis	0	(0.0)	1	(0.4)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.2)**	**1**	**(0.4)**
Asthma	0	(0.0)	1	(0.4)
Pleural effusion	1	(0.2)	0	(0.0)
Vascular disorders	**1**	**(0.2)**	**0**	**(0.0)**

Subjects With Serious Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n	(%)	n	(%)
Vascular disorders	**1**	**(0.2)**	**0**	**(0.0)**
Hypertensive crisis	1	(0.2)	0	(0.0)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 15

Subjects With Serious Drug-Related Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Overall Drug Related Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more serious drug-related adverse events	1	(0.2)	2	(0.8)	3	(0.4)
with no serious drug-related adverse events	530	(99.8)	264	(99.2)	794	(99.6)
Gastrointestinal disorders	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Vomiting	0	(0.0)	1	(0.4)	1	(0.1)
General disorders and administration site conditions	**0**	**(0.0)**	**1**	**(0.4)**	**1**	**(0.1)**
Drug ineffective	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Headache	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 16

Subjects With Serious Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more serious adverse events	35	(6.6)	30	(11.3)	65	(8.2)
with no serious adverse events	496	(93.4)	236	(88.7)	732	(91.8)
Cardiac disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Acute coronary syndrome	1	(0.2)	0	(0.0)	1	(0.1)
Gastrointestinal disorders	**5**	**(0.9)**	**3**	**(1.1)**	**8**	**(1.0)**
Enterocolitis	1	(0.2)	0	(0.0)	1	(0.1)
Gastritis	1	(0.2)	2	(0.8)	3	(0.4)
Gastrointestinal perforation	1	(0.2)	0	(0.0)	1	(0.1)
Proctitis	2	(0.4)	0	(0.0)	2	(0.3)
Vomiting	0	(0.0)	1	(0.4)	1	(0.1)
General disorders and administration site conditions	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
Drug ineffective	0	(0.0)	1	(0.4)	1	(0.1)
Peripheral swelling	1	(0.2)	0	(0.0)	1	(0.1)
Hepatobiliary disorders	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.4)**
Cholecystitis	1	(0.2)	0	(0.0)	1	(0.1)
Cholelithiasis	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis acute	1	(0.2)	0	(0.0)	1	(0.1)
Infections and infestations	**13**	**(2.4)**	**13**	**(4.9)**	**26**	**(3.3)**
Abdominal wall abscess	1	(0.2)	0	(0.0)	1	(0.1)
Acquired immunodeficiency syndrome	0	(0.0)	1	(0.4)	1	(0.1)
Appendicitis	0	(0.0)	1	(0.4)	1	(0.1)
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)	1	(0.1)
Dengue fever	1	(0.2)	0	(0.0)	1	(0.1)
Diarrhoea infectious	1	(0.2)	0	(0.0)	1	(0.1)
Diverticulitis	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis	2	(0.4)	1	(0.4)	3	(0.4)
Gastroenteritis bacterial	0	(0.0)	1	(0.4)	1	(0.1)
Gastroenteritis norovirus	1	(0.2)	0	(0.0)	1	(0.1)
Hepatitis C	1	(0.2)	0	(0.0)	1	(0.1)
Lymphogranuloma venereum	0	(0.0)	1	(0.4)	1	(0.1)
Osteomyelitis	0	(0.0)	1	(0.4)	1	(0.1)
Otitis externa	0	(0.0)	1	(0.4)	1	(0.1)
Perineal abscess	0	(0.0)	1	(0.4)	1	(0.1)
Pharyngitis	1	(0.2)	0	(0.0)	1	(0.1)
Pneumonia	1	(0.2)	0	(0.0)	1	(0.1)

Subjects With Serious Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**13**	**(2.4)**	**13**	**(4.9)**	**26**	**(3.3)**
Proctitis chlamydial	1	(0.2)	0	(0.0)	1	(0.1)
Subcutaneous abscess	0	(0.0)	1	(0.4)	1	(0.1)
Syphilis	1	(0.2)	0	(0.0)	1	(0.1)
Tuberculosis	1	(0.2)	1	(0.4)	2	(0.3)
Varicella	0	(0.0)	1	(0.4)	1	(0.1)
Vestibular neuronitis	1	(0.2)	0	(0.0)	1	(0.1)
Injury, poisoning and procedural complications	**2**	**(0.4)**	**4**	**(1.5)**	**6**	**(0.8)**
Alcohol poisoning	0	(0.0)	1	(0.4)	1	(0.1)
Foot fracture	0	(0.0)	1	(0.4)	1	(0.1)
Head injury	1	(0.2)	0	(0.0)	1	(0.1)
Joint dislocation	0	(0.0)	1	(0.4)	1	(0.1)
Post procedural haemorrhage	1	(0.2)	0	(0.0)	1	(0.1)
Tendon rupture	0	(0.0)	1	(0.4)	1	(0.1)
Musculoskeletal and connective tissue disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Back pain	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.4)**	**3**	**(1.1)**	**5**	**(0.6)**
Anogenital warts	1	(0.2)	0	(0.0)	1	(0.1)
Breast cancer in situ	0	(0.0)	1	(0.4)	1	(0.1)
Burkitt's lymphoma	0	(0.0)	1	(0.4)	1	(0.1)
Immunoblastic lymphoma	1	(0.2)	0	(0.0)	1	(0.1)
Queyrat erythroplasia	0	(0.0)	1	(0.4)	1	(0.1)
Nervous system disorders	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**
Cerebrovascular accident	0	(0.0)	1	(0.4)	1	(0.1)
Facial paresis	1	(0.2)	0	(0.0)	1	(0.1)
Headache	1	(0.2)	0	(0.0)	1	(0.1)
Ischaemic stroke	0	(0.0)	1	(0.4)	1	(0.1)
Transient ischaemic attack	1	(0.2)	0	(0.0)	1	(0.1)
Psychiatric disorders	**6**	**(1.1)**	**1**	**(0.4)**	**7**	**(0.9)**
Alcoholism	1	(0.2)	1	(0.4)	2	(0.3)
Depression	4	(0.8)	1	(0.4)	5	(0.6)
Mental status changes	1	(0.2)	0	(0.0)	1	(0.1)
Schizophrenia	1	(0.2)	0	(0.0)	1	(0.1)
Suicide attempt	1	(0.2)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**

Subjects With Serious Clinical Adverse Events
(Incidence > 0% in One or More Treatment Groups)
by System Organ Class
All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**3**	**(0.6)**	**2**	**(0.8)**	**5**	**(0.6)**
Acute kidney injury	0	(0.0)	1	(0.4)	1	(0.1)
Calculus urinary	1	(0.2)	1	(0.4)	2	(0.3)
Pollakiuria	1	(0.2)	0	(0.0)	1	(0.1)
Renal failure	1	(0.2)	0	(0.0)	1	(0.1)
Reproductive system and breast disorders	**0**	**(0.0)**	**2**	**(0.8)**	**2**	**(0.3)**
Benign prostatic hyperplasia	0	(0.0)	1	(0.4)	1	(0.1)
Prostatitis	0	(0.0)	1	(0.4)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.2)**	**2**	**(0.8)**	**3**	**(0.4)**
Asthma	0	(0.0)	1	(0.4)	1	(0.1)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.4)	1	(0.1)
Pleural effusion	1	(0.2)	0	(0.0)	1	(0.1)
Vascular disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Hypertensive crisis	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 17

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3066* Gender=[redacted], Race=[redacted], Age=28 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3066*	Treatment	103	Syphilis	2.86 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3067* Gender=[redacted], Race=[redacted], Age=59 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3067*	Treatment	116	Proctitis	1.18 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3068* Gender=[redacted] Race=[redacted], Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=425										
P3068*	Treatment	153	Proctitis chlamydial	8.97 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3069* Gender=[redacted], Race=[redacted], Age=60 Years, Rel Day of Last Recorded Dose of Study Medication=391										
P3069*	Treatment	197	Vestibular neuronitis	1.87 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3070* Gender=[redacted], Race=[redacted], Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=397										
P3070*	Treatment	244	Peripheral swelling	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3071* Gender=[redacted], Race=[redacted], Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=392										
P3071*	Treatment	350	Hypertensive crisis	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted], Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3073* Gender=[redacted], Race=[redacted], Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=36										
P3073*	Treatment	36	Immunoblastic lymphoma	1.51 Months	Severe	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		36	Renal failure	1.51 Months	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3074* Gender=[redacted] Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=475										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3074* Gender=[redacted], Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=475										
P3074*	Treatment	19	Transient ischaemic attack	3 Days	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3006* Gender=[redacted], Race=[redacted], Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=424										
P3006*	Treatment	162	Hepatitis acute	1.18 Months	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3075* Gender=[redacted] Race=[redacted], Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3075*	Treatment	343	Back pain	Continuing	Moderate	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3076* Gender=[redacted], Race=[redacted] Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=391										
P3076*	Treatment	184	Facial paresis	3.14 Weeks	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3077* Gender=[redacted], Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=453										
P3077*	Treatment	184	Gastrointestinal perforation	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3078* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=414										
P3078*	Treatment	38	Head injury	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3079* Gender=[redacted] Race=[redacted] Age=41 Years, Rel Day of Last Recorded Dose of Study Medication=333										
P3079*	Treatment	13	Gastroenteritis	3.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3005* Gender=[redacted] Race=[redacted] Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=512										
P3005*	Treatment	309	Alcoholism	Continuing	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3080* Gender=[redacted] Race=[redacted] Age=43 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3080*	Treatment	289	Gastroenteritis	6 Days	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3081* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3081*	Treatment	336	Post procedural haemorrhage	1.43 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3082* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=337										
P3082*	Treatment	37	Schizophrenia	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 1200.00 milligram
		118	Depression	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3082* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=337										
P3082*	Treatment	281	Proctitis	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3010* Gender=[redacted] Race=[redacted], Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=477										
P3010*	Treatment	184	Pharyngitis	1.43 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3083* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=462										
P3083*	Treatment	323	Diarrhoea infectious	1.14 Weeks	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3083* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=462										
P3083*	Treatment	331	Suicide attempt	Unknown	Severe	N	None	Unknown	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
		333	Depression	6 Days	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3084* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=491										
P3084*	Treatment	356	Depression	2 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3085* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=503										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3085* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=503										
P3085*	Treatment	378	Abdominal wall abscess	2 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3086* Gender=[redacted] Race=[redacted], Age=66 Years, Rel Day of Last Recorded Dose of Study Medication=463										
P3086*	Treatment	124	Acute coronary syndrome	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3087* Gender=[redacted] Race=[redacted] Age=59 Years, Rel Day of Last Recorded Dose of Study Medication=463										
P3087*	Treatment	349	Cholecystitis	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3088* Gender=[redacted] Race=[redacted] Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3088*	Treatment	311	Pneumonia	2.69 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		327	Pleural effusion	2.17 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3089* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=410										
P3089*	Treatment	279	Dengue fever	1.29 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3089* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=410										
P3089*	Treatment	292	Calculus urinary	5 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3090* Gender=[redacted] Race=[redacted] Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3090*	Treatment	289	Anogenital warts	2.33 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3091* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=399										
P3091*	Treatment	2	Headache	2 Days	Mild	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3063* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3063*	Treatment	1	Gastroenteritis norovirus	1.48 Months	Severe	N	Discontinued	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3002* Gender=[redacted] Race=[redacted] Age=46 Years, Rel Day of Last Recorded Dose of Study Medication=124										
P3002*	Treatment	121	Hepatitis C	Continuing	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3092* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=379										
P3092*	Treatment	261	Varicella	1.29 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3092* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=379										
P3092*	Treatment	261	Varicella	1.29 Weeks	Moderate	N	None	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3093* Gender=[redacted] Race=[redacted] Age=40 Years, Rel Day of Last Recorded Dose of Study Medication=469										
P3093*	Treatment	34	Otitis externa	1.51 Months	Mild	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3094* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=464										
P3094*	Treatment	264	Osteomyelitis	1.18 Months	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3095* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=504										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3095* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3095*	Treatment	361	Gastroenteritis	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3064* Gender=[redacted] Race=[redacted], Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=12										
P3064*	Treatment	1	Gastritis	1 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3096* Gender=[redacted] Race=[redacted] Age=27 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3096*	Treatment	191	Breast cancer in situ	4 Hours	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3097* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=475										
P3097*	Treatment	207	Alcohol poisoning	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
		207	Alcoholism	Continuing	Severe	N	None	Resolving	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
		207	Depression	Continuing	Severe	N	None	Resolving	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3098* Gender=[redacted] Race=[redacted] Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=422										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3098* Gender=[redacted] Race=[redacted] Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3098*	Treatment	64	Queyrat erythroplasia	1.51 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3099* Gender=[redacted] Race=[redacted] Age=34 Years, Rel Day of Last Recorded Dose of Study Medication=384										
P3099*	Treatment	125	Prostatitis	1.86 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3100* Gender=[redacted] Race=[redacted] Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3100*	Treatment	310	Foot fracture	1.71 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3101* Gender=[redacted] Race=[redacted] Age=50 Years, Rel Day of Last Recorded Dose of Study Medication=510										
P3101*	Treatment	13	Cerebral toxoplasmosis	1.05 Years	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3065* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=7										
P3065*	Treatment	8	Tuberculosis	Continuing	Severe	N	Discontinued	Not Resolved	1 day since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3052* Gender=[redacted] Race=[redacted] Age=56 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3052*	Treatment	287	Asthma	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3102* Gender=[redacted] Race=[redacted], Age=46 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3102*	Treatment	257	Drug ineffective	3 Weeks	Severe	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3102* Gender=[redacted] Race=[redacted], Age=46 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3102*	Treatment	257	Drug ineffective	3 Weeks	Severe	Y	None	Resolved	placebo (unspecified) raltegravir	0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3103* Gender=[redacted] Race=[redacted] Age=27 Years, Rel Day of Last Recorded Dose of Study Medication=413										
P3103*	Treatment	235	Gastritis	3.57 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3104* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=337										
P3104*	Treatment	42	Vomiting	4 Hours	Mild	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3105* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=204										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3105* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=204										
P3105*	Treatment	108	Burkitt's lymphoma	6.41 Months	Severe	N	Discontinued	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3106* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=421										
P3106*	Treatment	61	Tendon rupture	6.34 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3107* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=32										
P3107*	Treatment	17	Acquired immunodeficiency syndrome	1.12 Months	Severe	N	N/A	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3051* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=441										
P3051*	Treatment	241	Subcutaneous abscess	1 Weeks	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3108* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=338										
P3108*	Treatment	262	Gastroenteritis bacterial	1 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3109* Gender=[redacted] Race=[redacted] Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3109*	Treatment	118	Calculus urinary	1.25 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3110* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=336										
P3110*	Treatment	74	Perineal abscess	1.71 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3111* Gender=[redacted] Race=[redacted] Age=57 Years, Rel Day of Last Recorded Dose of Study Medication=459										
P3111*	Treatment	337	Benign prostatic hyperplasia	1.97 Months	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
		344	Acute kidney injury	1.74 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3112* Gender=[redacted] Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=343										

Listing of Subjects With Serious Clinical Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3112* Gender=[redacted] Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=343										
P3112*	Treatment	69	Lymphogranuloma venereum	1.14 Weeks	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram
		83	Lymphogranuloma venereum	2.71 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	800.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.
Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 18

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3066* Gender=[redacted] Race=[redacted] Age=28 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3066*	Treatment	103	Syphilis	2.86 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3067* Gender=[redacted] Race=[redacted] Age=59 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3067*	Treatment	116	Proctitis	1.18 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3068* Gender=[redacted] Race=[redacted], Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=425										
P3068*	Treatment	153	Proctitis chlamydial	8.97 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3069* Gender=[redacted] Race=[redacted], Age=60 Years, Rel Day of Last Recorded Dose of Study Medication=391										
P3069*	Treatment	197	Vestibular neuronitis	1.87 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3070* Gender=[redacted] Race=[redacted], Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=397										
P3070*	Treatment	244	Peripheral swelling	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3071* Gender=[redacted] Race=[redacted], Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=392										
P3071*	Treatment	350	Hypertensive crisis	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted] Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3073* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=36										
P3073*	Treatment	36	Immunoblastic lymphoma	1.51 Months	Severe	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		36	Renal failure	1.51 Months	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3074* Gender=[redacted] Race=[redacted] Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=475										

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3074* Gender=[redacted] Race=[redacted] Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=475										
P3074*	Treatment	19	Transient ischaemic attack	3 Days	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3006* Gender=[redacted] Race=[redacted] Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=424										
P3006*	Treatment	162	Hepatitis acute	1.18 Months	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3075* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3075*	Treatment	343	Back pain	Continuing	Moderate	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3113* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3113*	Treatment	488	Depression	Unknown	Severe	N	None	Unknown	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3076* Gender=[redacted] Race=[redacted] Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=391										
P3076*	Treatment	184	Facial paresis	3.14 Weeks	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3114* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=515										
P3114*	Treatment	500	Enterocolitis	Continuing	Severe	N	None	Resolving	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3077* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=453										
P3077*	Treatment	184	Gastrointestinal perforation	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3078* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=414										
P3078*	Treatment	38	Head injury	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3079* Gender=[redacted] Race=[redacted] Age=41 Years, Rel Day of Last Recorded Dose of Study Medication=333										
P3079*	Treatment	13	Gastroenteritis	3.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3005* Gender=[redacted] Race=[redacted] Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=512										
P3005*	Treatment	309	Alcoholism	Continuing	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3080* Gender=[redacted] Race=[redacted] Age=43 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3080*	Treatment	289	Gastroenteritis	6 Days	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3081* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3081*	Treatment	336	Post procedural haemorrhage	1.43 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3082* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=337										
P3082*	Treatment	37	Schizophrenia	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		118	Depression	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		281	Proctitis	3 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3115* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3115*	Treatment	424	Cholelithiasis	3.14 Weeks	Severe	N	None	Resolved	4 days since last dose	

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3010* Gender=[redacted] Race=[redacted], Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=477										
P3010*	Treatment	184	Pharyngitis	1.43 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
		425	Pollakiuria	5 Days	Mild	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	. milligram
									placebo (unspecified)	. milligram
									raltegravir	. milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3083* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=462										
P3083*	Treatment	323	Diarrhoea infectious	1.14 Weeks	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
		331	Suicide attempt	Unknown	Severe	N	None	Unknown	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3083* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=462										
P3083*	Treatment	333	Depression	6 Days	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	0.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3084* Gender=[redacted] Race=[redacted], Age=22 Years, Rel Day of Last Recorded Dose of Study Medication=491										
P3084*	Treatment	356	Depression	2 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3085* Gender=[redacted] Race=[redacted], Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=503										
P3085*	Treatment	378	Abdominal wall abscess	2 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3086* Gender=[redacted] Race=[redacted], Age=66 Years, Rel Day of Last Recorded Dose of Study Medication=463										
P3086*	Treatment	124	Acute coronary syndrome	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3116* Gender=[redacted] Race=[redacted], Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3116*	Treatment	421	Gastritis	2 Days	Severe	N	Interrupted	Resolved	1 day since last dose	
		423	Mental status changes	4 Days	Severe	N	Interrupted	Resolved	3 days since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3087* Gender=[redacted] Race=[redacted] Age=59 Years, Rel Day of Last Recorded Dose of Study Medication=463										
P3087*	Treatment	349	Cholecystitis	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3088* Gender=[redacted] Race=[redacted] Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=420										

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3088* Gender=[redacted] Race=[redacted] Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3088*	Treatment	311	Pneumonia	2.69 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
		327	Pleural effusion	2.17 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3089* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=410										
P3089*	Treatment	279	Dengue fever	1.29 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
									placebo (unspecified)	0.00 milligram
									raltegravir	1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3089* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=410										
P3089*	Treatment	292	Calculus urinary	5 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3090* Gender=[redacted] Race=[redacted] Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3090*	Treatment	289	Anogenital warts	2.33 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3091* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=399										
P3091*	Treatment	2	Headache	2 Days	Mild	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3063* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3063*	Treatment	1	Gastroenteritis norovirus	1.48 Months	Severe	N	Discontinued	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3002* Gender=[redacted] Race=[redacted] Age=46 Years, Rel Day of Last Recorded Dose of Study Medication=124										
P3002*	Treatment	121	Hepatitis C	Continuing	Severe	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3092* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=379										
P3092*	Treatment	261	Varicella	1.29 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3092* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=379										
P3092*	Treatment	261	Varicella	1.29 Weeks	Moderate	N	None	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3117* Gender=[redacted] Race=[redacted], Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=418										
P3117*	Treatment	411	Joint dislocation	Continuing	Severe	N	None	Not Resolved	placebo (unspecified) raltegravir	0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3093* Gender=[redacted] Race=[redacted] Age=40 Years, Rel Day of Last Recorded Dose of Study Medication=469										
P3093*	Treatment	34	Otitis externa	1.51 Months	Mild	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
		437	Chronic obstructive pulmonary disease	1.86 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3094* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=464										
P3094*	Treatment	264	Osteomyelitis	1.18 Months	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3095* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3095*	Treatment	361	Gastroenteritis	1.14 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3064* Gender=[redacted] Race=[redacted], Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=12										
P3064*	Treatment	1	Gastritis	1 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3096* Gender=[redacted] Race=[redacted] Age=27 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3096*	Treatment	191	Breast cancer in situ	4 Hours	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3097* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=475										
P3097*	Treatment	207	Alcohol poisoning	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
		207	Alcoholism	Continuing	Severe	N	None	Resolving	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3097* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=475										
P3097*	Treatment	207	Depression	Continuing	Severe	N	None	Resolving	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3098* Gender=[redacted] Race=[redacted] Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3098*	Treatment	64	Queyrat erythroplasia	1.51 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3099* Gender=[redacted] Race=[redacted] Age=34 Years, Rel Day of Last Recorded Dose of Study Medication=384										
P3099*	Treatment	125	Prostatitis	1.86 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3100* Gender=[redacted] Race=[redacted] Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=422										
P3100*	Treatment	310	Foot fracture	1.71 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3101* Gender=[redacted] Race=[redacted] Age=50 Years, Rel Day of Last Recorded Dose of Study Medication=510										
P3101*	Treatment	13	Cerebral toxoplasmosis	1.05 Years	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3118* Gender=[redacted] Race=[redacted] Age=37 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3118*	Treatment	470	Appendicitis	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3065* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=7										
P3065*	Treatment	8	Tuberculosis	Continuing	Severe	N	Discontinued	Not Resolved	1 day since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3052* Gender=[redacted] Race=[redacted] Age=56 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3052*	Treatment	287	Asthma	6 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3102* Gender=[redacted] Race=[redacted], Age=46 Years, Rel Day of Last Recorded Dose of Study Medication=487										
P3102*	Treatment	257	Drug ineffective	3 Weeks	Severe	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3103* Gender=[redacted] Race=[redacted] Age=27 Years, Rel Day of Last Recorded Dose of Study Medication=413										
P3103*	Treatment	235	Gastritis	3.57 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram

* 新薬承認情報提供時に置き換え

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3103* Gender=[redacted] Race=[redacted] Age=27 Years, Rel Day of Last Recorded Dose of Study Medication=413										
P3103*	Treatment	235	Gastritis	3.57 Weeks	Severe	N	None	Resolved	placebo (unspecified) raltegravir	0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3104* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=337										
P3104*	Treatment	42	Vomiting	4 Hours	Mild	Y	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3105* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=204										
P3105*	Treatment	108	Burkitt's lymphoma	6.41 Months	Severe	N	Discontinued	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3106* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=421										

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3106* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=421										
P3106*	Treatment	61	Tendon rupture	6.34 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3119* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=504										
P3119*	Treatment	505	Cerebrovascular accident	3 Days	Severe	N	None	Resolved	1 day since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3107* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=32										
P3107*	Treatment	17	Acquired immunodeficiency syndrome	1.12 Months	Severe	N	N/A	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	0.00 milligram 0.00 milligram 0.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3051* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=441										
P3051*	Treatment	241	Subcutaneous abscess	1 Weeks	Severe	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3051* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=441										
P3051*	Treatment	241	Subcutaneous abscess	1 Weeks	Severe	N	Interrupted	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3108* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=338										
P3108*	Treatment	262	Gastroenteritis bacterial	1 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3109* Gender=[redacted] Race=[redacted] Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=420										
P3109*	Treatment	118	Calculus urinary	1.25 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3120* Gender=[redacted] Race=[redacted] Age=43 Years, Rel Day of Last Recorded Dose of Study Medication=503										

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3120* Gender=[redacted] Race=[redacted] Age=43 Years, Rel Day of Last Recorded Dose of Study Medication=503										
P3120*	Treatment	465	Diverticulitis	2.14 Weeks	Moderate	N	Interrupted	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3110* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=336										
P3110*	Treatment	74	Perineal abscess	1.71 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3111* Gender=[redacted] Race=[redacted] Age=57 Years, Rel Day of Last Recorded Dose of Study Medication=459										
P3111*	Treatment	337	Benign prostatic hyperplasia	1.97 Months	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3111* Gender=[redacted] Race=[redacted] Age=57 Years, Rel Day of Last Recorded Dose of Study Medication=459										
P3111*	Treatment	344	Acute kidney injury	1.74 Months	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3121* Gender=[redacted] Race=[redacted] Age=43 Years, Rel Day of Last Recorded Dose of Study Medication=480										
P3121*	Treatment	477	Ischaemic stroke	4 Days	Severe	N	Unknown	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3112* Gender=[redacted] Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=343										
P3112*	Treatment	69	Lymphogranuloma venereum	1.14 Weeks	Severe	N	None	Sequelae	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Serious Clinical Adverse Events
All Data Available

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3112* Gender=[redacted] Race=[redacted], Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=343										
P3112*	Treatment	83	Lymphogranuloma venereum	2.71 Weeks	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

* 新薬承認情報提供時に置き換え

Table 2.7.4: 19

Listing of Subjects With Serious Laboratory Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3122* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=414										
P3122*	Treatment	50	Lipase increased	4 Days	Severe	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3123* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=392										
P3123*	Treatment	56	Aspartate aminotransferase increased	1.43 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
		56	Blood creatine phosphokinase increased	2.71 Weeks	Moderate	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Serious Laboratory Adverse Events
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3123* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=392										
P3123*	Treatment	56	Blood creatine phosphokinase increased	2.71 Weeks	Moderate	N	None	Resolved	raltegravir	1200.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.
Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 20

Listing of Subjects With Adverse Events Resulting in Death
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted] Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	Y	N	Discontinued	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3073* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=36										
P3073*	Treatment	36	Immunoblastic lymphoma	1.51 Months	Severe	Y	N	Discontinued	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3107* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=32										
P3107*	Treatment	17	Acquired immunodeficiency syndrome	1.12 Months	Severe	Y	N	N/A	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	0.00 milligram 0.00 milligram

Listing of Subjects With Adverse Events Resulting in Death
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3107* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=32										
P3107*	Treatment	17	Acquired immunodeficiency syndrome	1.12 Months	Severe	Y	N	N/A	raltegravir	0.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Related: Investigator-assessed relationship of the adverse event to study medication.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 21

Listing of Subjects With Clinical Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3001* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=17										
P3001*	Treatment	1	Hepatitis B	1.41 Months	Severe	N	N	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted] Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	Y	N	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3073* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=36										
P3073*	Treatment	36	Immunoblastic lymphoma	1.51 Months	Severe	Y	N	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3063* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=9										
P3063*	Treatment	1	Gastroenteritis norovirus	1.48 Months	Severe	Y	N	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3124* Gender=[redacted] Race=[redacted], Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=170										
P3124*	Treatment	121	Tuberculosis	Continuing	Moderate	N	N	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3125* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=18										
P3125*	Treatment	12	Syncope	2.43 Weeks	Mild	N	N	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Clinical Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3125* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=18										
P3125*	Treatment	12	Syncope	2.43 Weeks	Mild	N	N	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3065* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=7										
P3065*	Treatment	8	Tuberculosis	Continuing	Severe	Y	N	Not Resolved	1 day since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3105* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=204										
P3105*	Treatment	108	Burkitt's lymphoma	6.41 Months	Severe	Y	N	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3126* Gender=[redacted] Race=[redacted] Age=57 Years, Rel Day of Last Recorded Dose of Study Medication=331										
P3126*	Treatment	253	Thrombocytopenia	Continuing	Severe	N	Y	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Clinical Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3127* Gender=[redacted] Race=[redacted], Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=30										
P3127*	Treatment	15	Drug eruption	1.68 Months	Moderate	N	Y	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 22

Listing of Subjects With Laboratory Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3128* Gender=[redacted] Race=[redacted], Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=144										
P3128*	Treatment	142	Blood creatine phosphokinase increased	1.14 Weeks	Severe	N	Y	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3004* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=222										
P3004*	Treatment	169	Alanine aminotransferase increased	Continuing	Severe	N	Y	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
		169	Aspartate aminotransferase increased	Continuing	Moderate	N	Y	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Laboratory Adverse Events Resulting in Discontinuation
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD										
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3004* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=222										
P3004*	Treatment	169	Aspartate aminotransferase increased	Continuing	Moderate	N	Y	Not Resolved	raltegravir	1200.00 milligram

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 23

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - Immune Reconstitution Syndrome Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	11	(2.1)	3	(1.1)	14	(1.8)
with no adverse events	520	(97.9)	263	(98.9)	783	(98.2)
General disorders and administration site conditions	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Pyrexia	1	(0.2)	0	(0.0)	1	(0.1)
Infections and infestations	**6**	**(1.1)**	**2**	**(0.8)**	**8**	**(1.0)**
Conjunctivitis	1	(0.2)	0	(0.0)	1	(0.1)
Cytomegalovirus infection	1	(0.2)	0	(0.0)	1	(0.1)
Genital herpes zoster	1	(0.2)	0	(0.0)	1	(0.1)
Herpes zoster	3	(0.6)	2	(0.8)	5	(0.6)
Tuberculosis	1	(0.2)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.4)**	**1**	**(0.4)**	**3**	**(0.4)**
Anogenital warts	2	(0.4)	0	(0.0)	2	(0.3)
Keratoacanthoma	0	(0.0)	1	(0.4)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**
Cough	1	(0.2)	0	(0.0)	1	(0.1)
Skin and subcutaneous tissue disorders	**3**	**(0.6)**	**0**	**(0.0)**	**3**	**(0.4)**
Dermatitis	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophilic pustular folliculitis	1	(0.2)	0	(0.0)	1	(0.1)
Rash	1	(0.2)	0	(0.0)	1	(0.1)
Rash maculo-papular	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 24

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3062* Gender=[redacted] Race=[redacted] Age=41 Years, Rel Day of Last Recorded Dose of Study Medication=167											
P3062*	Treatment	21	Conjunctivitis	6 Days	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted] Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9											
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	Y	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3129* Gender=[redacted] Race=[redacted], Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=336											
P3129*	Treatment	38	Rash	2.29 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3129* Gender=[redacted] Race=[redacted], Age=42 Years, Rel Day of Last Recorded Dose of Study Medication=336											
P3129*	Treatment	38	Rash maculo-papular	3.14 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	1200.00 milligram
		38	Rash maculo-papular	3.14 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3130* Gender=[redacted] Race=[redacted] Age=25 Years, Rel Day of Last Recorded Dose of Study Medication=393											
P3130*	Treatment	223	Herpes zoster	1 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3003* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=384											

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3003* Gender=[redacted] Race=[redacted] Age=20 Years, Rel Day of Last Recorded Dose of Study Medication=384											
P3003*	Treatment	9	Eosinophilic pustular folliculitis	1.77 Months	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3131* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=392											
P3131*	Treatment	62	Anogenital warts	1.87 Months	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3079* Gender=[redacted] Race=[redacted] Age=41 Years, Rel Day of Last Recorded Dose of Study Medication=333											
P3079*	Treatment	287	Genital herpes zoster	1.71 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3079* Gender=[redacted] Race=[redacted] Age=41 Years, Rel Day of Last Recorded Dose of Study Medication=333											
P3079*	Treatment	287	Herpes zoster	1.71 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3132* Gender=[redacted], Race=[redacted] Age=47 Years, Rel Day of Last Recorded Dose of Study Medication=376											
P3132*	Treatment	37	Herpes zoster	3.29 Weeks	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3133* Gender=[redacted] Race=[redacted] Age=36 Years, Rel Day of Last Recorded Dose of Study Medication=504											
P3133*	Treatment	24	Cough	3.29 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3133* Gender=[redacted] Race=[redacted] Age=36 Years, Rel Day of Last Recorded Dose of Study Medication=504											
P3133*	Treatment	24	Pyrexia	3.29 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
		80	Dermatitis	2.2 Months	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3088* Gender=[redacted], Race=[redacted] Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3088*	Treatment	8	Anogenital warts	3.14 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3134* Gender=[redacted] Race=[redacted] Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=404											

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3134* Gender=[redacted] Race=[redacted] Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=404											
P3134*	Treatment	23	Cytomegalovirus infection	2 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3135* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=385											
P3135*	Treatment	10	Herpes zoster	1.57 Weeks	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3094* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=464											
P3094*	Treatment	79	Keratoacanthoma	7.66 Months	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Clinical Adverse Events - Immune Reconstitution Syndrome
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3094* Gender=[redacted] Race=[redacted] Age=45 Years, Rel Day of Last Recorded Dose of Study Medication=464											
P3094*	Treatment	79	Keratoacanthoma	7.66 Months	Moderate	N	N	None	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3136* Gender=[redacted] Race=[redacted], Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=336											
P3136*	Treatment	10	Herpes zoster	2 Weeks	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.
Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 25

Subjects With Clinical Adverse Events (Incidence > 0% in One or More Treatment Groups) by System Organ Class - AIDS Defining Conditions Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	7	(1.3)	6	(2.3)	13	(1.6)
with no adverse events	524	(98.7)	260	(97.7)	784	(98.4)
Infections and infestations	**6**	**(1.1)**	**5**	**(1.9)**	**11**	**(1.4)**
Cerebral toxoplasmosis	0	(0.0)	1	(0.4)	1	(0.1)
Cytomegalovirus infection	1	(0.2)	0	(0.0)	1	(0.1)
Herpes simplex	1	(0.2)	2	(0.8)	3	(0.4)
Oesophageal candidiasis	1	(0.2)	0	(0.0)	1	(0.1)
Pneumocystis jirovecii pneumonia	1	(0.2)	0	(0.0)	1	(0.1)
Tuberculosis	2	(0.4)	2	(0.8)	4	(0.5)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.2)**	**1**	**(0.4)**	**2**	**(0.3)**
Burkitt's lymphoma	0	(0.0)	1	(0.4)	1	(0.1)
Immunoblastic lymphoma	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 26

Listing of Subjects With Clinical Adverse Events - AIDS Defining Conditions
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3137* Gender=[redacted] Race=[redacted] Age=32 Years, Rel Day of Last Recorded Dose of Study Medication=405											
P3137*	Treatment	146	Tuberculosis	Continuing	Moderate	N	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3138* Gender=[redacted] Race=[redacted] Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3138*	Treatment	91	Oesophageal candidiasis	1.14 Weeks	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3139* Gender=[redacted] Race=[redacted], Age=32 Years, Rel Day of Last Recorded Dose of Study Medication=404											
P3139*	Treatment	5	Herpes simplex	2.14 Weeks	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - AIDS Defining Conditions
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3072* Gender=[redacted] Race=[redacted], Age=44 Years, Rel Day of Last Recorded Dose of Study Medication=9											
P3072*	Treatment	7	Tuberculosis	4.29 Weeks	Severe	Y	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3073* Gender=[redacted] Race=[redacted] Age=31 Years, Rel Day of Last Recorded Dose of Study Medication=36											
P3073*	Treatment	36	Immunoblastic lymphoma	1.51 Months	Severe	Y	N	Discontinued	Fatal	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3036* Gender=[redacted] Race=[redacted] Age=52 Years, Rel Day of Last Recorded Dose of Study Medication=421											
P3036*	Treatment	10	Pneumocystis jirovecii pneumonia	2.29 Weeks	Severe	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 0.00 milligram

Listing of Subjects With Clinical Adverse Events - AIDS Defining Conditions
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3134* Gender=[redacted] Race=[redacted] Age=38 Years, Rel Day of Last Recorded Dose of Study Medication=404											
P3134*	Treatment	23	Cytomegalovirus infection	2 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3124* Gender=[redacted] Race=[redacted], Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=170											
P3124*	Treatment	121	Tuberculosis	Continuing	Moderate	N	N	Discontinued	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3047* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=231											
P3047*	Treatment	134	Herpes simplex	3.25 Months	Moderate	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	500.00 milligram 0.00 milligram

Listing of Subjects With Clinical Adverse Events - AIDS Defining Conditions
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3047* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=231											
P3047*	Treatment	134	Herpes simplex	3.25 Months	Moderate	N	N	None	Resolved	raltegravir	800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3101* Gender=[redacted] Race=[redacted] Age=50 Years, Rel Day of Last Recorded Dose of Study Medication=510											
P3101*	Treatment	13	Cerebral toxoplasmosis	1.05 Years	Severe	Y	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3065* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=7											
P3065*	Treatment	8	Tuberculosis	Continuing	Severe	Y	N	Discontinued	Not Resolved	1 day since last dose	
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3105* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=204											
P3105*	Treatment	108	Burkitt's lymphoma	6.41 Months	Severe	Y	N	Discontinued	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Clinical Adverse Events - AIDS Defining Conditions
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3140* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3140*	Treatment	195	Herpes simplex	Continuing	Mild	N	N	None	Not Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 27

Summary of Laboratory Tests
Weeks 0-48

Week	Raltegravir 1200 mg QD			Raltegravir 400 mg BID		
	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Alkaline Phosphatase (IU/L)						
0	531	73.45		266	73.78	
1	505	73.39	-0.99 (12.45)	260	73.44	-1.20 (7.92)
2	516	73.83	0.78 (17.13)	251	73.61	0.45 (8.99)
4	526	73.56	4.07 (26.19)	261	73.25	2.05 (10.13)
8	523	73.46	5.22 (25.90)	259	72.97	4.24 (12.13)
16	510	73.55	7.86 (33.24)	257	73.01	4.72 (12.18)
24	510	73.41	7.85 (22.14)	254	72.35	5.83 (12.62)
36	498	73.18	9.79 (21.72)	249	72.12	7.83 (14.01)
48	493	73.23	10.02 (21.92)	246	72.06	8.04 (13.81)
Alanine Aminotransferase (IU/L)						
0	531	27.84		266	25.79	
1	505	28.06	-2.15 (33.56)	260	25.56	0.50 (8.92)
2	516	27.97	-0.52 (46.53)	251	26.12	-0.48 (11.71)
4	526	27.90	-1.43 (46.26)	261	25.97	-0.11 (14.81)
8	523	27.32	-1.81 (38.03)	259	25.99	0.16 (15.69)
16	510	27.46	1.40 (67.89)	257	26.13	1.01 (21.96)
24	510	27.45	-0.39 (41.73)	254	26.24	-0.24 (20.77)
36	498	27.56	-1.07 (40.78)	249	26.24	0.67 (20.41)
48	493	27.19	-0.13 (41.79)	246	26.27	-0.63 (17.47)
Aspartate Aminotransferase (IU/L)						
0	531	28.67		266	27.05	
1	505	28.73	-1.77 (38.54)	260	26.99	0.40 (7.84)
2	515	28.72	-1.04 (41.09)	250	27.13	0.58 (21.80)
4	523	28.70	-1.33 (42.65)	261	27.03	0.17 (13.55)
8	521	28.35	-2.06 (38.93)	258	27.09	-0.55 (10.67)
16	509	28.45	-1.01 (51.73)	256	27.15	0.15 (16.08)
24	509	28.39	-2.09 (41.24)	254	27.18	-1.69 (11.81)
36	497	28.27	-3.07 (39.40)	249	26.97	-0.31 (18.68)
48	492	28.18	-2.34 (40.92)	246	26.98	-2.06 (10.85)
Total Bilirubin (mg/dL)						
0	531	0.57		266	0.56	
1	505	0.56	-0.02 (0.21)	260	0.57	-0.03 (0.20)
2	515	0.56	-0.00 (0.22)	249	0.57	-0.03 (0.20)
4	523	0.57	0.02 (0.37)	261	0.56	-0.02 (0.21)
8	519	0.57	0.00 (0.29)	259	0.56	-0.01 (0.20)
16	510	0.57	0.04 (0.29)	257	0.56	0.03 (0.25)
24	509	0.57	0.03 (0.25)	254	0.56	0.04 (0.25)
36	498	0.56	0.05 (0.26)	249	0.56	0.05 (0.24)
48	493	0.57	0.07 (0.28)	246	0.56	0.06 (0.24)

Summary of Laboratory Tests
Weeks 0-48

Week	Raltegravir 1200 mg QD			Raltegravir 400 mg BID		
	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Creatine Kinase (IU/L)						
0	531	148.18		266	134.58	
1	505	149.20	-0.08 (375.25)	260	134.83	23.05 (292.39)
2	516	148.29	-2.39 (341.66)	251	136.03	149.67 (2081.15)
4	526	148.48	40.06 (650.22)	261	135.52	61.52 (644.05)
8	523	149.04	51.41 (909.89)	259	135.87	23.36 (222.69)
16	510	149.91	28.83 (468.53)	257	135.38	76.05 (502.85)
24	510	150.14	66.54 (880.75)	253	136.29	44.46 (286.99)
36	498	149.77	16.08 (414.50)	249	136.06	68.43 (374.88)
48	493	150.10	45.09 (642.83)	246	135.65	39.42 (275.44)
Creatinine (mg/dL)						
0	531	0.85		266	0.88	
1	505	0.85	0.05 (0.08)	260	0.88	0.05 (0.08)
2	516	0.85	0.06 (0.07)	251	0.89	0.05 (0.08)
4	526	0.85	0.06 (0.08)	261	0.88	0.06 (0.09)
8	523	0.85	0.06 (0.09)	259	0.88	0.06 (0.08)
16	510	0.85	0.06 (0.09)	257	0.88	0.06 (0.10)
24	510	0.85	0.05 (0.09)	253	0.88	0.07 (0.12)
36	498	0.85	0.07 (0.09)	249	0.88	0.07 (0.09)
48	493	0.85	0.07 (0.09)	246	0.88	0.08 (0.11)
Hemoglobin (gm/dL)						
0	531	14.12		266	14.20	
1	499	14.14	-0.03 (0.54)	255	14.21	-0.04 (0.58)
2	510	14.12	0.07 (0.60)	243	14.23	0.07 (0.67)
4	524	14.12	0.17 (0.66)	256	14.21	0.18 (0.75)
8	519	14.13	0.32 (0.73)	259	14.22	0.40 (0.84)
16	508	14.13	0.52 (0.85)	258	14.22	0.61 (0.90)
24	505	14.14	0.47 (0.84)	251	14.21	0.55 (0.89)
36	492	14.15	0.54 (0.88)	248	14.22	0.59 (0.94)
48	489	14.15	0.56 (0.94)	245	14.21	0.66 (0.96)
Lipase (IU/L)						
0	531	31.16		266	31.11	
1	505	31.28	2.55 (22.74)	260	31.08	2.68 (21.19)
2	516	31.12	3.17 (22.93)	251	31.49	1.47 (18.23)
4	525	31.10	0.66 (24.95)	261	31.20	1.07 (17.42)
8	523	31.02	0.19 (30.34)	260	31.20	0.53 (16.94)
16	513	30.90	-1.25 (34.52)	258	31.05	-2.38 (16.94)
24	509	30.96	-3.11 (29.18)	254	30.88	-1.70 (21.87)
36	497	30.97	-3.43 (28.00)	249	30.97	-2.65 (18.77)
48	493	31.08	-3.29 (24.34)	246	31.07	-2.73 (16.46)

Summary of Laboratory Tests
Weeks 0-48

Week	Raltegravir 1200 mg QD			Raltegravir 400 mg BID		
	N	Baseline Mean	Mean Change†(SD)	N	Baseline Mean	Mean Change†(SD)
Neutrophils (10[3]/microL)						
0	531	3.16		265	3.10	
1	494	3.15	0.08 (1.25)	251	3.13	0.10 (1.38)
2	500	3.15	0.33 (1.59)	239	3.09	0.28 (1.17)
4	518	3.16	0.13 (1.38)	254	3.10	0.29 (1.32)
8	508	3.14	0.20 (1.44)	256	3.10	0.17 (1.35)
16	502	3.15	0.26 (1.44)	250	3.10	0.42 (1.50)
24	502	3.14	0.35 (1.50)	248	3.07	0.40 (1.31)
36	485	3.14	0.39 (1.34)	245	3.09	0.60 (1.34)
48	487	3.16	0.44 (1.57)	244	3.10	0.63 (1.51)
Platelets (10[3]/microL)						
0	530	217.76		266	215.38	
1	495	218.54	13.69 (30.02)	255	214.61	11.50 (29.51)
2	506	217.98	17.79 (34.02)	242	217.02	16.42 (35.09)
4	520	218.14	17.81 (39.76)	256	215.49	16.72 (36.94)
8	515	217.94	23.50 (40.48)	259	215.89	21.02 (37.93)
16	503	218.37	24.89 (42.62)	257	215.47	19.72 (39.41)
24	499	217.77	28.37 (46.18)	251	215.27	22.27 (41.64)
36	489	218.86	26.45 (49.84)	245	217.22	24.21 (41.30)
48	483	219.10	29.61 (52.86)	243	217.58	24.70 (44.84)

†Change Scores are mean change from baseline and are based on the measurements of the subjects who were measured at baseline and the time point assessed.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of patients subjects in the treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 28

Analysis of Subjects With Laboratory Adverse Events (Incidence ≥1% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)†
Subjects in population	531		266		
with one or more adverse events	37	(7.0)	30	(11.3)	-4.3 (-9.1, -0.2)
with no adverse events	494	(93.0)	236	(88.7)	4.3 (0.2, 9.1)
Investigations	**37**	**(7.0)**	**30**	**(11.3)**	**-4.3 (-9.1, -0.2)**
Alanine aminotransferase increased	9	(1.7)	3	(1.1)	0.6 (-1.7, 2.3)
Aspartate aminotransferase increased	14	(2.6)	5	(1.9)	0.8 (-1.9, 2.8)
Blood creatine phosphokinase increased	18	(3.4)	17	(6.4)	-3.0 (-6.8, 0.0)
Lipase increased	4	(0.8)	5	(1.9)	-1.1 (-3.6, 0.4)

†Based on Miettinen & Nurminen method.

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Estimated differences and confidence intervals are provided in accordance with the statistical analysis plan.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 29

Analysis of Adverse Event Summary
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference in % vs Raltegravir 400 mg BID
	n	(%)	n	(%)	Estimate (95% CI)[†]
Subjects in population	531		266		
with one or more adverse events	37	(7.0)	30	(11.3)	-4.3 (-9.1, -0.2)
with no adverse events	494	(93.0)	236	(88.7)	4.3 (0.2, 9.1)
with drug-related[‡] adverse events	8	(1.5)	4	(1.5)	0.0 (-2.4, 1.7)
with serious adverse events	2	(0.4)	0	(0.0)	0.4 (-1.1, 1.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0.0 (-1.4, 0.7)
who died	0	(0.0)	0	(0.0)	0.0 (-1.4, 0.7)
discontinued[§] due to an adverse event	2	(0.4)	0	(0.0)	0.4 (-1.1, 1.4)
discontinued due to a drug-related adverse event	2	(0.4)	0	(0.0)	0.4 (-1.1, 1.4)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0.0 (-1.4, 0.7)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0.0 (-1.4, 0.7)

[†] Based on Miettinen & Nurminen method.
[‡] Determined by the investigator to be related to the drug.
[§] Study medication withdrawn.
Estimated differences and confidence intervals are provided in accordance with the statistical analysis plan.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 30

Subjects With Laboratory Adverse Events
(Incidence > 0% in One or More Treatment Groups)
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	37	(7.0)	30	(11.3)	67	(8.4)
with no adverse events	494	(93.0)	236	(88.7)	730	(91.6)
Investigations	**37**	**(7.0)**	**30**	**(11.3)**	**67**	**(8.4)**
Alanine aminotransferase increased	9	(1.7)	3	(1.1)	12	(1.5)
Amylase increased	1	(0.2)	0	(0.0)	1	(0.1)
Aspartate aminotransferase increased	14	(2.6)	5	(1.9)	19	(2.4)
Blood alkaline phosphatase increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood bilirubin increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	18	(3.4)	17	(6.4)	35	(4.4)
Blood creatinine increased	1	(0.2)	1	(0.4)	2	(0.3)
Blood glucose increased	2	(0.4)	1	(0.4)	3	(0.4)
Blood magnesium decreased	1	(0.2)	0	(0.0)	1	(0.1)
Blood phosphorus decreased	0	(0.0)	2	(0.8)	2	(0.3)
Blood phosphorus increased	0	(0.0)	1	(0.4)	1	(0.1)
Blood sodium decreased	1	(0.2)	0	(0.0)	1	(0.1)
CD4 lymphocyte percentage decreased	1	(0.2)	0	(0.0)	1	(0.1)
CD4 lymphocytes decreased	1	(0.2)	0	(0.0)	1	(0.1)
CD4/CD8 ratio decreased	1	(0.2)	0	(0.0)	1	(0.1)
Eosinophil count increased	3	(0.6)	1	(0.4)	4	(0.5)
Human papilloma virus test positive	0	(0.0)	1	(0.4)	1	(0.1)
Lipase increased	4	(0.8)	5	(1.9)	9	(1.1)
Neutrophil count decreased	1	(0.2)	1	(0.4)	2	(0.3)
Serum ferritin decreased	0	(0.0)	1	(0.4)	1	(0.1)
White blood cell count decreased	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 31

Adverse Event Summary
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	37	(7.0)	30	(11.3)	67	(8.4)
with no adverse event	494	(93.0)	236	(88.7)	730	(91.6)
with drug-related† adverse events	8	(1.5)	4	(1.5)	12	(1.5)
with serious adverse events	2	(0.4)	0	(0.0)	2	(0.3)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	2	(0.4)	0	(0.0)	2	(0.3)
discontinued due to a drug-related adverse event	2	(0.4)	0	(0.0)	2	(0.3)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 32

Adverse Event Summary
Laboratory Adverse Events
All Data Available

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more adverse events	44	(8.3)	30	(11.3)	74	(9.3)
with no adverse event	487	(91.7)	236	(88.7)	723	(90.7)
with drug-related† adverse events	8	(1.5)	4	(1.5)	12	(1.5)
with serious adverse events	2	(0.4)	0	(0.0)	2	(0.3)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	2	(0.4)	0	(0.0)	2	(0.3)
discontinued due to a drug-related adverse event	2	(0.4)	0	(0.0)	2	(0.3)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 33

Subjects With Drug-Related Laboratory Adverse Events by Drug Relationship (Incidence >0% in One or More Treatment Groups) Weeks 0-48

	Relationship	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
		n	(%)	n	(%)	n	(%)
Subjects in population		531		266		797	
With one or more drug-related adverse events	Overall	8	(1.5)	4	(1.5)	12	(1.5)
	Raltegravir	8	(1.5)	4	(1.5)	12	(1.5)
Investigations	**Overall**	**8**	**(1.5)**	**4**	**(1.5)**	**12**	**(1.5)**
	Raltegravir	8	(1.5)	4	(1.5)	12	(1.5)
Alanine aminotransferase increased	Overall	2	(0.4)	0	(0.0)	2	(0.3)
	Raltegravir	2	(0.4)	0	(0.0)	2	(0.3)
Aspartate aminotransferase increased	Overall	3	(0.6)	0	(0.0)	3	(0.4)
	Raltegravir	3	(0.6)	0	(0.0)	3	(0.4)
Blood creatine phosphokinase increased	Overall	5	(0.9)	3	(1.1)	8	(1.0)
	Raltegravir	5	(0.9)	3	(1.1)	8	(1.0)
Lipase increased	Overall	0	(0.0)	1	(0.4)	1	(0.1)
	Raltegravir	0	(0.0)	1	(0.4)	1	(0.1)

Every subject is counted once on each applicable row.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.

Relationship: study medication(s) to which the investigator attributed the adverse event. Raltegravir (alone or in combination with TRUVADA™), open label TRUVADA™ only.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 34

Subjects With Drug-Related Laboratory Adverse Events of Moderate or Severe Intensities
(Incidence > 0% in One or More Treatment Groups)
Overall Drug Related
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more drug-related adverse events	6	(1.1)	2	(0.8)	8	(1.0)
with no drug-related adverse events	525	(98.9)	264	(99.2)	789	(99.0)
Investigations	**6**	**(1.1)**	**2**	**(0.8)**	**8**	**(1.0)**
Alanine aminotransferase increased	2	(0.4)	0	(0.0)	2	(0.3)
Aspartate aminotransferase increased	2	(0.4)	0	(0.0)	2	(0.3)
Blood creatine phosphokinase increased	3	(0.6)	1	(0.4)	4	(0.5)
Lipase increased	0	(0.0)	1	(0.4)	1	(0.1)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 35

Subjects With Serious Drug-Related Laboratory Adverse Events
(Incidence > 0% in One or More Treatment Groups)
Overall Drug Related
Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)
with no serious drug-related adverse events	531	(100.0)	266	(100.0)	797	(100.0)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 36

Subjects With Serious Laboratory Adverse Events (Incidence > 0% in One or More Treatment Groups) Weeks 0-48

	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	531		266		797	
with one or more serious adverse events	2	(0.4)	0	(0.0)	2	(0.3)
with no serious adverse events	529	(99.6)	266	(100.0)	795	(99.7)
Investigations	**2**	**(0.4)**	**0**	**(0.0)**	**2**	**(0.3)**
Aspartate aminotransferase increased	1	(0.2)	0	(0.0)	1	(0.1)
Blood creatine phosphokinase increased	1	(0.2)	0	(0.0)	1	(0.1)
Lipase increased	1	(0.2)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable row and column.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 37

Analysis of Subjects With Laboratory Findings That Met Predetermined Criteria
(Incidence ≥1% in One or More Treatment Groups)
Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD n/m	(%)	Raltegravir 400 mg BID n/m	(%)	Difference [QD – BID]‡ % (95% CI)
HEMATOLOGY					
Neutrophils (10[3]/microL)					
Grade 1:1.00 - 1.30	21/530	(4.0)	10/265	(3.8)	0.2 (-3.1, 2.9)
Grade 2:0.75 - 0.999	7/530	(1.3)	2/265	(0.8)	0.6 (-1.5, 2.1)
Grade 3:0.50 - 0.749	5/530	(0.9)	3/265	(1.1)	-0.2 (-2.4, 1.3)
Platelets (10[3]/microL)					
Grade 1:100 - 124.999	7/529	(1.3)	5/266	(1.9)	-0.6 (-3.1, 1.2)
CHEMISTRY					
Total Bilirubin (mg/dL)					
Grade 1:1.1 - 1.5 x ULN	27/530	(5.1)	14/266	(5.3)	-0.2 (-3.9, 2.9)
Grade 2:1.6 - 2.5 x ULN	7/530	(1.3)	2/266	(0.8)	0.6 (-1.5, 2.1)
Creatinine (mg/dL)					
Grade 1:1.1 - 1.3 x ULN	4/530	(0.8)	3/266	(1.1)	-0.4 (-2.6, 1.0)
Aspartate Aminotransferase (IU/L)					
Grade 1:1.25 - 2.5 x ULN	39/530	(7.4)	29/266	(10.9)	-3.5 (-8.3, 0.5)
Grade 2:2.6 - 5.0 x ULN	16/530	(3.0)	5/266	(1.9)	1.1 (-1.5, 3.3)
Grade 3:5.1 - 10.0 x ULN	6/530	(1.1)	1/266	(0.4)	0.8 (-1.0, 2.1)
Alanine Aminotransferase (IU/L)					
Grade 1:1.25 - 2.5 x ULN	49/530	(9.2)	33/266	(12.4)	-3.2 (-8.2, 1.3)
Grade 2:2.6 - 5.0 x ULN	13/530	(2.5)	2/266	(0.8)	1.7 (-0.4, 3.5)
Alkaline Phosphatase (IU/L)					
Grade 1:1.25 - 2.5 x ULN	12/530	(2.3)	3/266	(1.1)	1.1 (-1.2, 3.0)
Grade 2:2.6 - 5.0 x ULN	6/530	(1.1)	0/266	(0.0)	1.1 (-0.3, 2.4)

Analysis of Subjects With Laboratory Findings That Met Predetermined Criteria (Incidence ≥1% in One or More Treatment Groups) Worsening Grade; Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Difference [QD – BID][‡]
	n/m	(%)	n/m	(%)	% (95% CI)
Lipase (IU/L)					
Grade 1:1.1 - 1.5 x ULN	35/530	(6.6)	25/266	(9.4)	-2.8 (-7.3, 1.0)
Grade 2:1.6 - 3.0 x ULN	27/530	(5.1)	12/266	(4.5)	0.6 (-3.0, 3.5)
Grade 3:3.1 - 5.0 x ULN	8/530	(1.5)	1/266	(0.4)	1.1 (-0.7, 2.6)
Creatine Kinase (IU/L)					
Grade 1:3.0 - 5.9 x ULN	31/530	(5.8)	20/266	(7.5)	-1.7 (-5.8, 1.8)
Grade 2:6.0 - 9.9 x ULN	17/530	(3.2)	6/266	(2.3)	1.0 (-1.9, 3.2)
Grade 3:10.0 - 19.9 x ULN	6/530	(1.1)	7/266	(2.6)	-1.5 (-4.3, 0.4)
Grade 4:>= 20.0 x ULN	10/530	(1.9)	4/266	(1.5)	0.4 (-2.1, 2.2)

[†] For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A patient was listed with a Grade X event if his/her highest grade during treatment was X.

[‡] The 95% CIs for the treatment differences in percent with PDLC were calculated using Miettinen and Nurminen method.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 38

Listing of Liver Function Laboratory Values
Subjects With Aminotransferase (ALT or AST) ≥3 x ULN and Bilirubin ≥2 x ULN and Alkaline Phosphatase <2 x ULN
Weeks 0-48

Subject ID	Epoch	Relative Day	Relative Day Within Epoch	Test	Result	Normal Range Lower	Normal Range Upper	Criteria Met
Treatment: Raltegravir 1200 mg QD								
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3001* Gender=[redacted] Race=[redacted] Age=31 Years, Relative Day of Study Medication Discontinuance†=17								
P3001*	Screening	-28	11617	ALT	30 IU/L	0	48	
				AST	26 IU/L	0	42	
				BILI	.6 mg/dL	0	1.3	
				ALP	84 IU/L	20	125	
		1	11645	ALT	338 IU/L	0	48	
				AST	215 IU/L	0	42	
				BILI	.7 mg/dL	0	1.3	
				ALP	109 IU/L	20	125	
	Treatment	8	8	ALT	566 IU/L	0	48	
				AST	459 IU/L	0	42	
				BILI	1.1 mg/dL	0	1.3	
				ALP	195 IU/L	20	125	
		15	15	ALT	998 IU/L	0	48	Yes
				AST	565 IU/L	0	42	Yes
				BILI	2.8 mg/dL	0	1.3	Yes
				ALP	205 IU/L	20	125	Yes
		28	28	ALT	1001 IU/L	0	48	Yes
				AST	683 IU/L	0	42	Yes
				BILI	7.6 mg/dL	0	1.3	Yes

Listing of Liver Function Laboratory Values
Subjects With Aminotransferase (ALT or AST) ≥3 x ULN and Bilirubin ≥2 x ULN and Alkaline Phosphatase <2 x ULN
Weeks 0-48

Subject ID	Epoch	Relative Day	Relative Day Within Epoch	Test	Result	Normal Range		Criteria Met
						Lower	Upper	
Treatment: Raltegravir 1200 mg QD								
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3001* Gender=[redacted] Race=[redacted] Age=31 Years, Relative Day of Study Medication Discontinuance†=17								
P3001*	Treatment	28	28	ALP	163 IU/L	20	125	Yes

†Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the subject relative to the start of study medication.
Relative Day is the day of laboratory sample collection relative to the start of study medication.
Relative Day within Epoch is the day of laboratory sample collection relative to the start of the Epoch.
If the lab criteria were met on a specific day, all results for that day are flagged as having met the criteria.
The baseline test result is the result from the latest sample before/at Day 1.
ALP = Alkaline phosphatase; ALT = Alanine aminotransferase; AST = Aspartate aminotransferase; BILI = Bilirubin; ULN = Upper limit of normal range.
Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 39

Subjects With Laboratory Findings That Met Predetermined Criteria
Grade 2 or Greater
Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n/m	(%)	n/m	(%)
HEMATOLOGY				
Neutrophils (10[3]/microL)				
Grade 2:0.75 - 0.999	7/530	(1.3)	2/265	(0.8)
Grade 3:0.50 - 0.749	5/530	(0.9)	3/265	(1.1)
Grade 4:<0.50	0/530	(0.0)	0/265	(0.0)
Hemoglobin (gm/dL)				
Grade 2:7.5 - 8.4	0/530	(0.0)	0/266	(0.0)
Grade 3:6.5 - 7.4	0/530	(0.0)	0/266	(0.0)
Grade 4:< 6.5	0/530	(0.0)	0/266	(0.0)
Platelets (10[3]/microL)				
Grade 2:50 - 99.999	4/529	(0.8)	1/266	(0.4)
Grade 3:25 - 49.999	0/529	(0.0)	0/266	(0.0)
Grade 4:<25	0/529	(0.0)	1/266	(0.4)
CHEMISTRY				
Total Bilirubin (mg/dL)				
Grade 2:1.6 - 2.5 x ULN	7/530	(1.3)	2/266	(0.8)
Grade 3:2.6 - 5.0 x ULN	3/530	(0.6)	0/266	(0.0)
Grade 4:>5.0 x ULN	1/530	(0.2)	0/266	(0.0)
Creatinine (mg/dL)				
Grade 2:1.4 - 1.8 x ULN	0/530	(0.0)	1/266	(0.4)
Grade 3:1.9 - 3.4 x ULN	0/530	(0.0)	0/266	(0.0)
Grade 4:>=3.5 x ULN	0/530	(0.0)	0/266	(0.0)
Aspartate Aminotransferase (IU/L)				
Grade 2:2.6 - 5.0 x ULN	16/530	(3.0)	5/266	(1.9)
Grade 3:5.1 - 10.0 x ULN	6/530	(1.1)	1/266	(0.4)
Grade 4:>10.0 x ULN	2/530	(0.4)	0/266	(0.0)
Alanine Aminotransferase (IU/L)				
Grade 2:2.6 - 5.0 x ULN	13/530	(2.5)	2/266	(0.8)
Grade 3:5.1 - 10.0 x ULN	5/530	(0.9)	1/266	(0.4)
Grade 4:>10.0 x ULN	2/530	(0.4)	0/266	(0.0)
Alkaline Phosphatase (IU/L)				
Grade 2:2.6 - 5.0 x ULN	6/530	(1.1)	0/266	(0.0)
Grade 3:5.1 - 10.0 x ULN	0/530	(0.0)	0/266	(0.0)
Grade 4:>10.0 x ULN	0/530	(0.0)	0/266	(0.0)

Subjects With Laboratory Findings That Met Predetermined Criteria
Grade 2 or Greater
Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID	
	n/m	(%)	n/m	(%)
Lipase (IU/L)				
Grade 2:1.6 - 3.0 x ULN	27/530	(5.1)	12/266	(4.5)
Grade 3:3.1 - 5.0 x ULN	8/530	(1.5)	1/266	(0.4)
Grade 4:>5.0 x ULN	5/530	(0.9)	0/266	(0.0)
Creatine Kinase (IU/L)				
Grade 2:6.0 - 9.9 x ULN	17/530	(3.2)	6/266	(2.3)
Grade 3:10.0 - 19.9 x ULN	6/530	(1.1)	7/266	(2.6)
Grade 4:>= 20.0 x ULN	10/530	(1.9)	4/266	(1.5)

† For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A patient was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 40

Subjects With Laboratory Findings That Met Predetermined Criteria Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
HEMATOLOGY						
Neutrophils (10[3]/microL)						
Grade 1:1.00 - 1.30	21/530	(4.0)	10/265	(3.8)	31/795	(3.9)
Grade 2:0.75 - 0.999	7/530	(1.3)	2/265	(0.8)	9/795	(1.1)
Grade 3:0.50 - 0.749	5/530	(0.9)	3/265	(1.1)	8/795	(1.0)
Grade 4:<0.50	0/530	(0.0)	0/265	(0.0)	0/795	(0.0)
Hemoglobin (gm/dL)						
Grade 1:8.5 - 10.0	5/530	(0.9)	1/266	(0.4)	6/796	(0.8)
Grade 2:7.5 - 8.4	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Grade 3:6.5 - 7.4	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Grade 4:< 6.5	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Platelets (10[3]/microL)						
Grade 1:100 - 124.999	7/529	(1.3)	5/266	(1.9)	12/795	(1.5)
Grade 2:50 - 99.999	4/529	(0.8)	1/266	(0.4)	5/795	(0.6)
Grade 3:25 - 49.999	0/529	(0.0)	0/266	(0.0)	0/795	(0.0)
Grade 4:<25	0/529	(0.0)	1/266	(0.4)	1/795	(0.1)
CHEMISTRY						
Total Bilirubin (mg/dL)						
Grade 1:1.1 - 1.5 x ULN	27/530	(5.1)	14/266	(5.3)	41/796	(5.2)
Grade 2:1.6 - 2.5 x ULN	7/530	(1.3)	2/266	(0.8)	9/796	(1.1)
Grade 3:2.6 - 5.0 x ULN	3/530	(0.6)	0/266	(0.0)	3/796	(0.4)
Grade 4:>5.0 x ULN	1/530	(0.2)	0/266	(0.0)	1/796	(0.1)
Creatinine (mg/dL)						
Grade 1:1.1 - 1.3 x ULN	4/530	(0.8)	3/266	(1.1)	7/796	(0.9)
Grade 2:1.4 - 1.8 x ULN	0/530	(0.0)	1/266	(0.4)	1/796	(0.1)
Grade 3:1.9 - 3.4 x ULN	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Grade 4:≥3.5 x ULN	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Aspartate Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	39/530	(7.4)	29/266	(10.9)	68/796	(8.5)
Grade 2:2.6 - 5.0 x ULN	16/530	(3.0)	5/266	(1.9)	21/796	(2.6)
Grade 3:5.1 - 10.0 x ULN	6/530	(1.1)	1/266	(0.4)	7/796	(0.9)
Grade 4:>10.0 x ULN	2/530	(0.4)	0/266	(0.0)	2/796	(0.3)
Alanine Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	49/530	(9.2)	33/266	(12.4)	82/796	(10.3)
Grade 2:2.6 - 5.0 x ULN	13/530	(2.5)	2/266	(0.8)	15/796	(1.9)
Grade 3:5.1 - 10.0 x ULN	5/530	(0.9)	1/266	(0.4)	6/796	(0.8)
Grade 4:>10.0 x ULN	2/530	(0.4)	0/266	(0.0)	2/796	(0.3)

Subjects With Laboratory Findings That Met Predetermined Criteria Worsening Grade; Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
Alkaline Phosphatase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	12/530	(2.3)	3/266	(1.1)	15/796	(1.9)
Grade 2:2.6 - 5.0 x ULN	6/530	(1.1)	0/266	(0.0)	6/796	(0.8)
Grade 3:5.1 - 10.0 x ULN	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Grade 4:>10.0 x ULN	0/530	(0.0)	0/266	(0.0)	0/796	(0.0)
Lipase (IU/L)						
Grade 1:1.1 - 1.5 x ULN	35/530	(6.6)	25/266	(9.4)	60/796	(7.5)
Grade 2:1.6 - 3.0 x ULN	27/530	(5.1)	12/266	(4.5)	39/796	(4.9)
Grade 3:3.1 - 5.0 x ULN	8/530	(1.5)	1/266	(0.4)	9/796	(1.1)
Grade 4:>5.0 x ULN	5/530	(0.9)	0/266	(0.0)	5/796	(0.6)
Creatine Kinase (IU/L)						
Grade 1:3.0 - 5.9 x ULN	31/530	(5.8)	20/266	(7.5)	51/796	(6.4)
Grade 2:6.0 - 9.9 x ULN	17/530	(3.2)	6/266	(2.3)	23/796	(2.9)
Grade 3:10.0 - 19.9 x ULN	6/530	(1.1)	7/266	(2.6)	13/796	(1.6)
Grade 4:≥ 20.0 x ULN	10/530	(1.9)	4/266	(1.5)	14/796	(1.8)

[†]For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A subject was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 41

Adverse Event Summary by Age
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	18 to 64		>=65		18 to 64		>=65		18 to 64		>=65	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	527		4		263		3		790		7	
with one or more adverse events	436	(82.7)	3	(75.0)	229	(87.1)	2	(66.7)	665	(84.2)	5	(71.4)
with no adverse event	91	(17.3)	1	(25.0)	34	(12.9)	1	(33.3)	125	(15.8)	2	(28.6)
with drug-related[†] adverse events	130	(24.7)	0	(0.0)	68	(25.9)	0	(0.0)	198	(25.1)	0	(0.0)
with serious adverse events	30	(5.7)	1	(25.0)	25	(9.5)	0	(0.0)	55	(7.0)	1	(14.3)
with serious drug-related adverse events	1	(0.2)	0	(0.0)	2	(0.8)	0	(0.0)	3	(0.4)	0	(0.0)
who died	2	(0.4)	0	(0.0)	1	(0.4)	0	(0.0)	3	(0.4)	0	(0.0)
discontinued[‡] due to an adverse event	4	(0.8)	0	(0.0)	6	(2.3)	0	(0.0)	10	(1.3)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.8)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	3	(0.6)	0	(0.0)	2	(0.8)	0	(0.0)	5	(0.6)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 42

Subjects With Clinical Adverse Events by Age (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	18 To 64		>=65		18 To 64		>=65		18 To 64		>=65	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	527		4		263		3		790		7	
with one or more adverse events	436	(82.7)	3	(75.0)	229	(87.1)	2	(66.7)	665	(84.2)	5	(71.4)
with no adverse events	91	(17.3)	1	(25.0)	34	(12.9)	1	(33.3)	125	(15.8)	2	(28.6)
Cardiac disorders	**4**	**(0.8)**	**1**	**(25.0)**	**3**	**(1.1)**	**0**	**(0.0)**	**7**	**(0.9)**	**1**	**(14.3)**
Acute coronary syndrome	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Eye disorders	**17**	**(3.2)**	**0**	**(0.0)**	**8**	**(3.0)**	**1**	**(33.3)**	**25**	**(3.2)**	**1**	**(14.3)**
Cataract	1	(0.2)	0	(0.0)	1	(0.4)	1	(33.3)	2	(0.3)	1	(14.3)
Gastrointestinal disorders	**209**	**(39.7)**	**0**	**(0.0)**	**99**	**(37.6)**	**0**	**(0.0)**	**308**	**(39.0)**	**0**	**(0.0)**
Abdominal pain	40	(7.6)	0	(0.0)	11	(4.2)	0	(0.0)	51	(6.5)	0	(0.0)
Diarrhoea	58	(11.0)	0	(0.0)	30	(11.4)	0	(0.0)	88	(11.1)	0	(0.0)
Nausea	60	(11.4)	0	(0.0)	26	(9.9)	0	(0.0)	86	(10.9)	0	(0.0)
Vomiting	35	(6.6)	0	(0.0)	15	(5.7)	0	(0.0)	50	(6.3)	0	(0.0)
General disorders and administration site conditions	**82**	**(15.6)**	**2**	**(50.0)**	**49**	**(18.6)**	**0**	**(0.0)**	**131**	**(16.6)**	**2**	**(28.6)**
Chest pain	5	(0.9)	1	(25.0)	2	(0.8)	0	(0.0)	7	(0.9)	1	(14.3)
Fatigue	32	(6.1)	1	(25.0)	16	(6.1)	0	(0.0)	48	(6.1)	1	(14.3)
Infections and infestations	**268**	**(50.9)**	**3**	**(75.0)**	**148**	**(56.3)**	**2**	**(66.7)**	**416**	**(52.7)**	**5**	**(71.4)**
Bronchitis	16	(3.0)	1	(25.0)	10	(3.8)	0	(0.0)	26	(3.3)	1	(14.3)
Chikungunya virus infection	2	(0.4)	0	(0.0)	1	(0.4)	1	(33.3)	3	(0.4)	1	(14.3)
Herpes zoster	8	(1.5)	2	(50.0)	3	(1.1)	0	(0.0)	11	(1.4)	2	(28.6)
Influenza	17	(3.2)	1	(25.0)	12	(4.6)	0	(0.0)	29	(3.7)	1	(14.3)

Subjects With Clinical Adverse Events by Age (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	18 To 64		>=65		18 To 64		>=65		18 To 64		>=65	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**268**	**(50.9)**	**3**	**(75.0)**	**148**	**(56.3)**	**2**	**(66.7)**	**416**	**(52.7)**	**5**	**(71.4)**
Nasopharyngitis	44	(8.3)	0	(0.0)	22	(8.4)	0	(0.0)	66	(8.4)	0	(0.0)
Proctitis chlamydial	4	(0.8)	0	(0.0)	2	(0.8)	1	(33.3)	6	(0.8)	1	(14.3)
Syphilis	14	(2.7)	0	(0.0)	14	(5.3)	0	(0.0)	28	(3.5)	0	(0.0)
Upper respiratory tract infection	40	(7.6)	0	(0.0)	19	(7.2)	0	(0.0)	59	(7.5)	0	(0.0)
Injury, poisoning and procedural complications	**56**	**(10.6)**	**1**	**(25.0)**	**28**	**(10.6)**	**0**	**(0.0)**	**84**	**(10.6)**	**1**	**(14.3)**
Wound secretion	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Investigations	**10**	**(1.9)**	**2**	**(50.0)**	**5**	**(1.9)**	**0**	**(0.0)**	**15**	**(1.9)**	**2**	**(28.6)**
Blood pressure decreased	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Blood pressure increased	4	(0.8)	1	(25.0)	0	(0.0)	0	(0.0)	4	(0.5)	1	(14.3)
Metabolism and nutrition disorders	**27**	**(5.1)**	**0**	**(0.0)**	**12**	**(4.6)**	**1**	**(33.3)**	**39**	**(4.9)**	**1**	**(14.3)**
Type 2 diabetes mellitus	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	1	(14.3)
Musculoskeletal and connective tissue disorders	**87**	**(16.5)**	**2**	**(50.0)**	**35**	**(13.3)**	**1**	**(33.3)**	**122**	**(15.4)**	**3**	**(42.9)**
Costochondritis	2	(0.4)	1	(25.0)	0	(0.0)	0	(0.0)	2	(0.3)	1	(14.3)
Myalgia	19	(3.6)	0	(0.0)	6	(2.3)	1	(33.3)	25	(3.2)	1	(14.3)
Pain in extremity	10	(1.9)	1	(25.0)	4	(1.5)	0	(0.0)	14	(1.8)	1	(14.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**25**	**(4.7)**	**0**	**(0.0)**	**9**	**(3.4)**	**1**	**(33.3)**	**34**	**(4.3)**	**1**	**(14.3)**
Uterine leiomyoma	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	1	(14.3)
Nervous system disorders	**122**	**(23.1)**	**0**	**(0.0)**	**54**	**(20.5)**	**0**	**(0.0)**	**176**	**(22.3)**	**0**	**(0.0)**

Subjects With Clinical Adverse Events by Age (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	18 To 64		>=65		18 To 64		>=65		18 To 64		>=65	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**122**	**(23.1)**	**0**	**(0.0)**	**54**	**(20.5)**	**0**	**(0.0)**	**176**	**(22.3)**	**0**	**(0.0)**
Headache	71	(13.5)	0	(0.0)	29	(11.0)	0	(0.0)	100	(12.7)	0	(0.0)
Psychiatric disorders	**70**	**(13.3)**	**1**	**(25.0)**	**43**	**(16.3)**	**0**	**(0.0)**	**113**	**(14.3)**	**1**	**(14.3)**
Depressed mood	1	(0.2)	1	(25.0)	0	(0.0)	0	(0.0)	1	(0.1)	1	(14.3)
Libido decreased	3	(0.6)	1	(25.0)	1	(0.4)	0	(0.0)	4	(0.5)	1	(14.3)
Reproductive system and breast disorders	**34**	**(6.5)**	**1**	**(25.0)**	**9**	**(3.4)**	**0**	**(0.0)**	**43**	**(5.4)**	**1**	**(14.3)**
Penile discharge	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Testicular swelling	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Respiratory, thoracic and mediastinal disorders	**76**	**(14.4)**	**0**	**(0.0)**	**40**	**(15.2)**	**0**	**(0.0)**	**116**	**(14.7)**	**0**	**(0.0)**
Cough	28	(5.3)	0	(0.0)	14	(5.3)	0	(0.0)	42	(5.3)	0	(0.0)
Skin and subcutaneous tissue disorders	**100**	**(19.0)**	**1**	**(25.0)**	**63**	**(24.0)**	**0**	**(0.0)**	**163**	**(20.6)**	**1**	**(14.3)**
Acne	9	(1.7)	1	(25.0)	3	(1.1)	0	(0.0)	12	(1.5)	1	(14.3)
Pruritus	15	(2.8)	0	(0.0)	15	(5.7)	0	(0.0)	30	(3.8)	0	(0.0)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 43

Adverse Event Summary by Age
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	18 to 64		>=65		18 to 64		>=65		18 to 64		>=65	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	527		4		263		3		790		7	
with one or more adverse events	37	(7.0)	0	(0.0)	30	(11.4)	0	(0.0)	67	(8.5)	0	(0.0)
with no adverse event	490	(93.0)	4	(100.0)	233	(88.6)	3	(100.0)	723	(91.5)	7	(100.0)
with drug-related[†] adverse events	8	(1.5)	0	(0.0)	4	(1.5)	0	(0.0)	12	(1.5)	0	(0.0)
with serious adverse events	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a drug-related adverse event	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 44

Adverse Event Summary by Gender
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	M		F		M		F		M		F	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	440		91		234		32		674		123	
with one or more adverse events	363	(82.5)	76	(83.5)	204	(87.2)	27	(84.4)	567	(84.1)	103	(83.7)
with no adverse event	77	(17.5)	15	(16.5)	30	(12.8)	5	(15.6)	107	(15.9)	20	(16.3)
with drug-related[†] adverse events	105	(23.9)	25	(27.5)	58	(24.8)	10	(31.3)	163	(24.2)	35	(28.5)
with serious adverse events	27	(6.1)	4	(4.4)	24	(10.3)	1	(3.1)	51	(7.6)	5	(4.1)
with serious drug-related adverse events	1	(0.2)	0	(0.0)	2	(0.9)	0	(0.0)	3	(0.4)	0	(0.0)
who died	1	(0.2)	1	(1.1)	1	(0.4)	0	(0.0)	2	(0.3)	1	(0.8)
discontinued[‡] due to an adverse event	3	(0.7)	1	(1.1)	5	(2.1)	1	(3.1)	8	(1.2)	2	(1.6)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.9)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	2	(0.5)	1	(1.1)	2	(0.9)	0	(0.0)	4	(0.6)	1	(0.8)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
M = Male; F = Female
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 45

Subjects With Clinical Adverse Events by Gender (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	M		F		M		F		M		F	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	440		91		234		32		674		123	
with one or more adverse events	363	(82.5)	76	(83.5)	204	(87.2)	27	(84.4)	567	(84.1)	103	(83.7)
with no adverse events	77	(17.5)	15	(16.5)	30	(12.8)	5	(15.6)	107	(15.9)	20	(16.3)
Blood and lymphatic system disorders	**19**	**(4.3)**	**5**	**(5.5)**	**8**	**(3.4)**	**0**	**(0.0)**	**27**	**(4.0)**	**5**	**(4.1)**
Ear and labyrinth disorders	**11**	**(2.5)**	**3**	**(3.3)**	**6**	**(2.6)**	**2**	**(6.3)**	**17**	**(2.5)**	**5**	**(4.1)**
Ear pain	3	(0.7)	2	(2.2)	2	(0.9)	2	(6.3)	5	(0.7)	4	(3.3)
Eye disorders	**14**	**(3.2)**	**3**	**(3.3)**	**7**	**(3.0)**	**2**	**(6.3)**	**21**	**(3.1)**	**5**	**(4.1)**
Gastrointestinal disorders	**167**	**(38.0)**	**42**	**(46.2)**	**86**	**(36.8)**	**13**	**(40.6)**	**253**	**(37.5)**	**55**	**(44.7)**
Abdominal pain	32	(7.3)	8	(8.8)	9	(3.8)	2	(6.3)	41	(6.1)	10	(8.1)
Diarrhoea	50	(11.4)	8	(8.8)	22	(9.4)	8	(25.0)	72	(10.7)	16	(13.0)
Gastrooesophageal reflux disease	8	(1.8)	0	(0.0)	6	(2.6)	2	(6.3)	14	(2.1)	2	(1.6)
Nausea	44	(10.0)	16	(17.6)	20	(8.5)	6	(18.8)	64	(9.5)	22	(17.9)
Vomiting	24	(5.5)	11	(12.1)	12	(5.1)	3	(9.4)	36	(5.3)	14	(11.4)
General disorders and administration site conditions	**71**	**(16.1)**	**13**	**(14.3)**	**45**	**(19.2)**	**4**	**(12.5)**	**116**	**(17.2)**	**17**	**(13.8)**
Fatigue	26	(5.9)	7	(7.7)	14	(6.0)	2	(6.3)	40	(5.9)	9	(7.3)
Infections and infestations	**222**	**(50.5)**	**49**	**(53.8)**	**133**	**(56.8)**	**17**	**(53.1)**	**355**	**(52.7)**	**66**	**(53.7)**
Bronchitis	12	(2.7)	5	(5.5)	8	(3.4)	2	(6.3)	20	(3.0)	7	(5.7)
Gastroenteritis	11	(2.5)	5	(5.5)	11	(4.7)	0	(0.0)	22	(3.3)	5	(4.1)
Nasopharyngitis	38	(8.6)	6	(6.6)	20	(8.5)	2	(6.3)	58	(8.6)	8	(6.5)

Subjects With Clinical Adverse Events by Gender (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	M		F		M		F		M		F	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**222**	**(50.5)**	**49**	**(53.8)**	**133**	**(56.8)**	**17**	**(53.1)**	**355**	**(52.7)**	**66**	**(53.7)**
Respiratory tract infection viral	1	(0.2)	3	(3.3)	1	(0.4)	3	(9.4)	2	(0.3)	6	(4.9)
Rhinitis	5	(1.1)	4	(4.4)	3	(1.3)	2	(6.3)	8	(1.2)	6	(4.9)
Syphilis	14	(3.2)	0	(0.0)	14	(6.0)	0	(0.0)	28	(4.2)	0	(0.0)
Upper respiratory tract infection	28	(6.4)	12	(13.2)	18	(7.7)	1	(3.1)	46	(6.8)	13	(10.6)
Vulvovaginal candidiasis	0	(0.0)	5	(5.5)	0	(0.0)	1	(3.1)	0	(0.0)	6	(4.9)
Injury, poisoning and procedural complications	**48**	**(10.9)**	**9**	**(9.9)**	**25**	**(10.7)**	**3**	**(9.4)**	**73**	**(10.8)**	**12**	**(9.8)**
Metabolism and nutrition disorders	**20**	**(4.5)**	**7**	**(7.7)**	**11**	**(4.7)**	**2**	**(6.3)**	**31**	**(4.6)**	**9**	**(7.3)**
Musculoskeletal and connective tissue disorders	**66**	**(15.0)**	**23**	**(25.3)**	**33**	**(14.1)**	**3**	**(9.4)**	**99**	**(14.7)**	**26**	**(21.1)**
Arthralgia	11	(2.5)	5	(5.5)	6	(2.6)	0	(0.0)	17	(2.5)	5	(4.1)
Back pain	19	(4.3)	5	(5.5)	7	(3.0)	1	(3.1)	26	(3.9)	6	(4.9)
Myalgia	14	(3.2)	5	(5.5)	6	(2.6)	1	(3.1)	20	(3.0)	6	(4.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**24**	**(5.5)**	**1**	**(1.1)**	**8**	**(3.4)**	**2**	**(6.3)**	**32**	**(4.7)**	**3**	**(2.4)**
Nervous system disorders	**98**	**(22.3)**	**24**	**(26.4)**	**49**	**(20.9)**	**5**	**(15.6)**	**147**	**(21.8)**	**29**	**(23.6)**
Dizziness	19	(4.3)	5	(5.5)	9	(3.8)	3	(9.4)	28	(4.2)	8	(6.5)
Headache	56	(12.7)	15	(16.5)	27	(11.5)	2	(6.3)	83	(12.3)	17	(13.8)
Psychiatric disorders	**67**	**(15.2)**	**4**	**(4.4)**	**39**	**(16.7)**	**4**	**(12.5)**	**106**	**(15.7)**	**8**	**(6.5)**
Depression	13	(3.0)	1	(1.1)	9	(3.8)	2	(6.3)	22	(3.3)	3	(2.4)
Insomnia	21	(4.8)	0	(0.0)	11	(4.7)	2	(6.3)	32	(4.7)	2	(1.6)

Subjects With Clinical Adverse Events by Gender (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	M		F		M		F		M		F	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**21**	**(4.8)**	**14**	**(15.4)**	**6**	**(2.6)**	**3**	**(9.4)**	**27**	**(4.0)**	**17**	**(13.8)**
Vaginal discharge	0	(0.0)	5	(5.5)	0	(0.0)	0	(0.0)	0	(0.0)	5	(4.1)
Respiratory, thoracic and mediastinal disorders	**62**	**(14.1)**	**14**	**(15.4)**	**37**	**(15.8)**	**3**	**(9.4)**	**99**	**(14.7)**	**17**	**(13.8)**
Cough	22	(5.0)	6	(6.6)	14	(6.0)	0	(0.0)	36	(5.3)	6	(4.9)
Skin and subcutaneous tissue disorders	**84**	**(19.1)**	**17**	**(18.7)**	**57**	**(24.4)**	**6**	**(18.8)**	**141**	**(20.9)**	**23**	**(18.7)**
Pruritus	13	(3.0)	2	(2.2)	13	(5.6)	2	(6.3)	26	(3.9)	4	(3.3)
Rash	17	(3.9)	6	(6.6)	11	(4.7)	0	(0.0)	28	(4.2)	6	(4.9)
Rash papular	3	(0.7)	5	(5.5)	3	(1.3)	1	(3.1)	6	(0.9)	6	(4.9)
Vascular disorders	**22**	**(5.0)**	**3**	**(3.3)**	**10**	**(4.3)**	**1**	**(3.1)**	**32**	**(4.7)**	**4**	**(3.3)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
M=Male; F=Female
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 46

Adverse Event Summary by Gender
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	M		F		M		F		M		F	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	440		91		234		32		674		123	
with one or more adverse events	35	(8.0)	2	(2.2)	29	(12.4)	1	(3.1)	64	(9.5)	3	(2.4)
with no adverse event	405	(92.0)	89	(97.8)	205	(87.6)	31	(96.9)	610	(90.5)	120	(97.6)
with drug-related[†] adverse events	8	(1.8)	0	(0.0)	4	(1.7)	0	(0.0)	12	(1.8)	0	(0.0)
with serious adverse events	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a drug-related adverse event	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
M = Male; F = Female
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 47

Adverse Event Summary by Ethnicity
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown		Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	126		380		19		6		52		205		8		1	
with one or more adverse events	111	(88.1)	311	(81.8)	11	(57.9)	6	(100.0)	44	(84.6)	178	(86.8)	8	(100.0)	1	(100.0)
with no adverse event	15	(11.9)	69	(18.2)	8	(42.1)	0	(0.0)	8	(15.4)	27	(13.2)	0	(0.0)	0	(0.0)
with drug-related[†] adverse events	38	(30.2)	89	(23.4)	2	(10.5)	1	(16.7)	10	(19.2)	57	(27.8)	1	(12.5)	0	(0.0)
with serious adverse events	2	(1.6)	29	(7.6)	0	(0.0)	0	(0.0)	4	(7.7)	20	(9.8)	1	(12.5)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)	1	(12.5)	0	(0.0)
who died	1	(0.8)	1	(0.3)	0	(0.0)	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	2	(1.6)	2	(0.5)	0	(0.0)	0	(0.0)	1	(1.9)	5	(2.4)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.9)	1	(0.5)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	1	(0.8)	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Event Summary by Ethnicity
Clinical Adverse Events
Weeks 0-48

	Total							
	Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	178		585		27		7	
with one or more adverse events	155	(87.1)	489	(83.6)	19	(70.4)	7	(100.0)
with no adverse event	23	(12.9)	96	(16.4)	8	(29.6)	0	(0.0)
with drug-related[†] adverse events	48	(27.0)	146	(25.0)	3	(11.1)	1	(14.3)
with serious adverse events	6	(3.4)	49	(8.4)	1	(3.7)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	2	(0.3)	1	(3.7)	0	(0.0)
who died	2	(1.1)	1	(0.2)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	3	(1.7)	7	(1.2)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	1	(0.6)	1	(0.2)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	1	(0.6)	4	(0.7)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 48

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	126		380		19		6		52		205		8		1	
with one or more adverse events	111	(88.1)	311	(81.8)	11	(57.9)	6	(100.0)	44	(84.6)	178	(86.8)	8	(100.0)	1	(100.0)
with no adverse events	15	(11.9)	69	(18.2)	8	(42.1)	0	(0.0)	8	(15.4)	27	(13.2)	0	(0.0)	0	(0.0)
Blood and lymphatic system disorders	**6**	**(4.8)**	**17**	**(4.5)**	**1**	**(5.3)**	**0**	**(0.0)**	**2**	**(3.8)**	**6**	**(2.9)**	**0**	**(0.0)**	**0**	**(0.0)**
Neutropenia	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Eye disorders	**2**	**(1.6)**	**15**	**(3.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(5.8)**	**6**	**(2.9)**	**0**	**(0.0)**	**0**	**(0.0)**
Gastrointestinal disorders	**51**	**(40.5)**	**146**	**(38.4)**	**8**	**(42.1)**	**4**	**(66.7)**	**11**	**(21.2)**	**85**	**(41.5)**	**2**	**(25.0)**	**1**	**(100.0)**
Abdominal distension	6	(4.8)	3	(0.8)	0	(0.0)	1	(16.7)	0	(0.0)	8	(3.9)	0	(0.0)	0	(0.0)
Abdominal pain	11	(8.7)	28	(7.4)	0	(0.0)	1	(16.7)	2	(3.8)	9	(4.4)	0	(0.0)	0	(0.0)
Abdominal pain lower	0	(0.0)	2	(0.5)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Abdominal pain upper	1	(0.8)	11	(2.9)	1	(5.3)	0	(0.0)	0	(0.0)	4	(2.0)	0	(0.0)	0	(0.0)
Constipation	3	(2.4)	10	(2.6)	1	(5.3)	0	(0.0)	0	(0.0)	4	(2.0)	0	(0.0)	0	(0.0)
Diarrhoea	20	(15.9)	37	(9.7)	1	(5.3)	0	(0.0)	1	(1.9)	28	(13.7)	0	(0.0)	1	(100.0)
Epigastric discomfort	0	(0.0)	1	(0.3)	1	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Flatulence	1	(0.8)	3	(0.8)	1	(5.3)	0	(0.0)	1	(1.9)	8	(3.9)	0	(0.0)	0	(0.0)
Gastritis	1	(0.8)	1	(0.3)	1	(5.3)	0	(0.0)	1	(1.9)	5	(2.4)	0	(0.0)	0	(0.0)
Gastrooesophageal reflux disease	3	(2.4)	3	(0.8)	1	(5.3)	1	(16.7)	0	(0.0)	8	(3.9)	0	(0.0)	0	(0.0)
Gingival bleeding	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Mouth ulceration	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Nausea	11	(8.7)	47	(12.4)	1	(5.3)	1	(16.7)	4	(7.7)	20	(9.8)	1	(12.5)	1	(100.0)
Proctalgia	1	(0.8)	1	(0.3)	1	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	178		585		27		7	
with one or more adverse events	155	(87.1)	489	(83.6)	19	(70.4)	7	(100.0)
with no adverse events	23	(12.9)	96	(16.4)	8	(29.6)	0	(0.0)
Blood and lymphatic system disorders	**8**	**(4.5)**	**23**	**(3.9)**	**1**	**(3.7)**	**0**	**(0.0)**
Neutropenia	0	(0.0)	0	(0.0)	1	(3.7)	0	(0.0)
Eye disorders	**5**	**(2.8)**	**21**	**(3.6)**	**0**	**(0.0)**	**0**	**(0.0)**
Gastrointestinal disorders	**62**	**(34.8)**	**231**	**(39.5)**	**10**	**(37.0)**	**5**	**(71.4)**
Abdominal distension	6	(3.4)	11	(1.9)	0	(0.0)	1	(14.3)
Abdominal pain	13	(7.3)	37	(6.3)	0	(0.0)	1	(14.3)
Abdominal pain lower	0	(0.0)	2	(0.3)	0	(0.0)	1	(14.3)
Abdominal pain upper	1	(0.6)	15	(2.6)	1	(3.7)	0	(0.0)
Constipation	3	(1.7)	14	(2.4)	1	(3.7)	0	(0.0)
Diarrhoea	21	(11.8)	65	(11.1)	1	(3.7)	1	(14.3)
Epigastric discomfort	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)
Flatulence	2	(1.1)	11	(1.9)	1	(3.7)	0	(0.0)
Gastritis	2	(1.1)	6	(1.0)	1	(3.7)	0	(0.0)
Gastrooesophageal reflux disease	3	(1.7)	11	(1.9)	1	(3.7)	1	(14.3)
Gingival bleeding	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Mouth ulceration	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)
Nausea	15	(8.4)	67	(11.5)	2	(7.4)	2	(28.6)
Proctalgia	1	(0.6)	1	(0.2)	1	(3.7)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**51**	**(40.5)**	**146**	**(38.4)**	**8**	**(42.1)**	**4**	**(66.7)**	**11**	**(21.2)**	**85**	**(41.5)**	**2**	**(25.0)**	**1**	**(100.0)**
Proctitis	2	(1.6)	2	(0.5)	0	(0.0)	1	(16.7)	1	(1.9)	3	(1.5)	0	(0.0)	0	(0.0)
Rectal haemorrhage	2	(1.6)	1	(0.3)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rectal stenosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tooth disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Toothache	2	(1.6)	5	(1.3)	1	(5.3)	1	(16.7)	0	(0.0)	4	(2.0)	1	(12.5)	0	(0.0)
Vomiting	7	(5.6)	27	(7.1)	1	(5.3)	0	(0.0)	1	(1.9)	13	(6.3)	1	(12.5)	0	(0.0)
General disorders and administration site conditions	**12**	**(9.5)**	**72**	**(18.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(9.6)**	**43**	**(21.0)**	**1**	**(12.5)**	**0**	**(0.0)**
Fatigue	6	(4.8)	27	(7.1)	0	(0.0)	0	(0.0)	2	(3.8)	14	(6.8)	0	(0.0)	0	(0.0)
Influenza like illness	0	(0.0)	9	(2.4)	0	(0.0)	0	(0.0)	1	(1.9)	9	(4.4)	1	(12.5)	0	(0.0)
Immune system disorders	**2**	**(1.6)**	**5**	**(1.3)**	**0**	**(0.0)**	**2**	**(33.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
House dust allergy	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Seasonal allergy	1	(0.8)	3	(0.8)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infections and infestations	**72**	**(57.1)**	**188**	**(49.5)**	**7**	**(36.8)**	**4**	**(66.7)**	**32**	**(61.5)**	**112**	**(54.6)**	**5**	**(62.5)**	**1**	**(100.0)**
Bronchitis	3	(2.4)	13	(3.4)	0	(0.0)	1	(16.7)	3	(5.8)	7	(3.4)	0	(0.0)	0	(0.0)
Epididymitis	1	(0.8)	2	(0.5)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Gastroenteritis	1	(0.8)	14	(3.7)	0	(0.0)	1	(16.7)	3	(5.8)	8	(3.9)	0	(0.0)	0	(0.0)
Gingivitis	0	(0.0)	3	(0.8)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Gonorrhoea	0	(0.0)	4	(1.1)	1	(5.3)	0	(0.0)	0	(0.0)	3	(1.5)	0	(0.0)	0	(0.0)
Herpes simplex	1	(0.8)	1	(0.3)	0	(0.0)	1	(16.7)	0	(0.0)	4	(2.0)	0	(0.0)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**62**	**(34.8)**	**231**	**(39.5)**	**10**	**(37.0)**	**5**	**(71.4)**
Proctitis	3	(1.7)	5	(0.9)	0	(0.0)	1	(14.3)
Rectal haemorrhage	2	(1.1)	1	(0.2)	0	(0.0)	1	(14.3)
Rectal stenosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Tooth disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Toothache	2	(1.1)	9	(1.5)	2	(7.4)	1	(14.3)
Vomiting	8	(4.5)	40	(6.8)	2	(7.4)	0	(0.0)
General disorders and administration site conditions	**17**	**(9.6)**	**115**	**(19.7)**	**1**	**(3.7)**	**0**	**(0.0)**
Fatigue	8	(4.5)	41	(7.0)	0	(0.0)	0	(0.0)
Influenza like illness	1	(0.6)	18	(3.1)	1	(3.7)	0	(0.0)
Immune system disorders	**2**	**(1.1)**	**5**	**(0.9)**	**0**	**(0.0)**	**2**	**(28.6)**
House dust allergy	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Seasonal allergy	1	(0.6)	3	(0.5)	0	(0.0)	1	(14.3)
Infections and infestations	**104**	**(58.4)**	**300**	**(51.3)**	**12**	**(44.4)**	**5**	**(71.4)**
Bronchitis	6	(3.4)	20	(3.4)	0	(0.0)	1	(14.3)
Epididymitis	1	(0.6)	3	(0.5)	1	(3.7)	0	(0.0)
Gastroenteritis	4	(2.2)	22	(3.8)	0	(0.0)	1	(14.3)
Gingivitis	0	(0.0)	4	(0.7)	1	(3.7)	0	(0.0)
Gonorrhoea	0	(0.0)	7	(1.2)	1	(3.7)	0	(0.0)
Herpes simplex	1	(0.6)	5	(0.9)	0	(0.0)	1	(14.3)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**72**	**(57.1)**	**188**	**(49.5)**	**7**	**(36.8)**	**4**	**(66.7)**	**32**	**(61.5)**	**112**	**(54.6)**	**5**	**(62.5)**	**1**	**(100.0)**
Influenza	7	(5.6)	11	(2.9)	0	(0.0)	0	(0.0)	5	(9.6)	7	(3.4)	0	(0.0)	0	(0.0)
Laryngitis	0	(0.0)	0	(0.0)	2	(10.5)	0	(0.0)	0	(0.0)	0	(0.0)	2	(25.0)	0	(0.0)
Localised infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Lymphogranuloma venereum	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Nasopharyngitis	9	(7.1)	30	(7.9)	4	(21.1)	1	(16.7)	2	(3.8)	16	(7.8)	3	(37.5)	1	(100.0)
Pharyngitis	6	(4.8)	8	(2.1)	0	(0.0)	0	(0.0)	4	(7.7)	4	(2.0)	0	(0.0)	0	(0.0)
Pneumonia bacterial	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)
Respiratory tract infection	0	(0.0)	5	(1.3)	0	(0.0)	1	(16.7)	0	(0.0)	2	(1.0)	0	(0.0)	0	(0.0)
Syphilis	0	(0.0)	13	(3.4)	1	(5.3)	0	(0.0)	1	(1.9)	13	(6.3)	0	(0.0)	0	(0.0)
Tooth abscess	1	(0.8)	1	(0.3)	0	(0.0)	1	(16.7)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Upper respiratory tract infection	6	(4.8)	32	(8.4)	1	(5.3)	1	(16.7)	5	(9.6)	13	(6.3)	1	(12.5)	0	(0.0)
Urethritis	0	(0.0)	8	(2.1)	1	(5.3)	0	(0.0)	1	(1.9)	6	(2.9)	0	(0.0)	0	(0.0)
Urinary tract infection	3	(2.4)	8	(2.1)	0	(0.0)	0	(0.0)	1	(1.9)	1	(0.5)	1	(12.5)	0	(0.0)
Injury, poisoning and procedural complications	**13**	**(10.3)**	**43**	**(11.3)**	**1**	**(5.3)**	**0**	**(0.0)**	**6**	**(11.5)**	**22**	**(10.7)**	**0**	**(0.0)**	**0**	**(0.0)**
Accidental overdose	3	(2.4)	18	(4.7)	1	(5.3)	0	(0.0)	2	(3.8)	8	(3.9)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders	**7**	**(5.6)**	**20**	**(5.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(3.8)**	**11**	**(5.4)**	**0**	**(0.0)**	**0**	**(0.0)**
Musculoskeletal and connective tissue disorders	**24**	**(19.0)**	**64**	**(16.8)**	**0**	**(0.0)**	**1**	**(16.7)**	**7**	**(13.5)**	**27**	**(13.2)**	**1**	**(12.5)**	**1**	**(100.0)**
Back pain	7	(5.6)	17	(4.5)	0	(0.0)	0	(0.0)	0	(0.0)	6	(2.9)	1	(12.5)	1	(100.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**104**	**(58.4)**	**300**	**(51.3)**	**12**	**(44.4)**	**5**	**(71.4)**
Influenza	12	(6.7)	18	(3.1)	0	(0.0)	0	(0.0)
Laryngitis	0	(0.0)	0	(0.0)	4	(14.8)	0	(0.0)
Localised infection	0	(0.0)	1	(0.2)	0	(0.0)	1	(14.3)
Lymphogranuloma venereum	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)
Nasopharyngitis	11	(6.2)	46	(7.9)	7	(25.9)	2	(28.6)
Pharyngitis	10	(5.6)	12	(2.1)	0	(0.0)	0	(0.0)
Pneumonia bacterial	0	(0.0)	0	(0.0)	1	(3.7)	0	(0.0)
Respiratory tract infection	0	(0.0)	7	(1.2)	0	(0.0)	1	(14.3)
Syphilis	1	(0.6)	26	(4.4)	1	(3.7)	0	(0.0)
Tooth abscess	1	(0.6)	2	(0.3)	0	(0.0)	1	(14.3)
Upper respiratory tract infection	11	(6.2)	45	(7.7)	2	(7.4)	1	(14.3)
Urethritis	1	(0.6)	14	(2.4)	1	(3.7)	0	(0.0)
Urinary tract infection	4	(2.2)	9	(1.5)	1	(3.7)	0	(0.0)
Injury, poisoning and procedural complications	**19**	**(10.7)**	**65**	**(11.1)**	**1**	**(3.7)**	**0**	**(0.0)**
Accidental overdose	5	(2.8)	26	(4.4)	1	(3.7)	0	(0.0)
Metabolism and nutrition disorders	**9**	**(5.1)**	**31**	**(5.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Musculoskeletal and connective tissue disorders	**31**	**(17.4)**	**91**	**(15.6)**	**1**	**(3.7)**	**2**	**(28.6)**
Back pain	7	(3.9)	23	(3.9)	1	(3.7)	1	(14.3)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**24**	**(19.0)**	**64**	**(16.8)**	**0**	**(0.0)**	**1**	**(16.7)**	**7**	**(13.5)**	**27**	**(13.2)**	**1**	**(12.5)**	**1**	**(100.0)**
Joint swelling	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)
Myalgia	3	(2.4)	15	(3.9)	0	(0.0)	1	(16.7)	3	(5.8)	4	(2.0)	0	(0.0)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**6**	**(4.8)**	**17**	**(4.5)**	**1**	**(5.3)**	**1**	**(16.7)**	**4**	**(7.7)**	**6**	**(2.9)**	**0**	**(0.0)**	**0**	**(0.0)**
Papilloma	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Thyroid neoplasm	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	**35**	**(27.8)**	**81**	**(21.3)**	**5**	**(26.3)**	**1**	**(16.7)**	**11**	**(21.2)**	**41**	**(20.0)**	**2**	**(25.0)**	**0**	**(0.0)**
Dizziness	6	(4.8)	18	(4.7)	0	(0.0)	0	(0.0)	1	(1.9)	11	(5.4)	0	(0.0)	0	(0.0)
Headache	22	(17.5)	44	(11.6)	5	(26.3)	0	(0.0)	9	(17.3)	19	(9.3)	1	(12.5)	0	(0.0)
Hypoaesthesia	0	(0.0)	2	(0.5)	0	(0.0)	0	(0.0)	1	(1.9)	3	(1.5)	1	(12.5)	0	(0.0)
Paraesthesia	2	(1.6)	1	(0.3)	0	(0.0)	1	(16.7)	0	(0.0)	2	(1.0)	0	(0.0)	0	(0.0)
Psychiatric disorders	**19**	**(15.1)**	**49**	**(12.9)**	**2**	**(10.5)**	**1**	**(16.7)**	**9**	**(17.3)**	**33**	**(16.1)**	**1**	**(12.5)**	**0**	**(0.0)**
Abnormal dreams	0	(0.0)	12	(3.2)	2	(10.5)	1	(16.7)	1	(1.9)	6	(2.9)	0	(0.0)	0	(0.0)
Insomnia	6	(4.8)	13	(3.4)	1	(5.3)	1	(16.7)	3	(5.8)	9	(4.4)	1	(12.5)	0	(0.0)
Renal and urinary disorders	**3**	**(2.4)**	**9**	**(2.4)**	**1**	**(5.3)**	**0**	**(0.0)**	**2**	**(3.8)**	**4**	**(2.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Pollakiuria	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**31**	**(17.4)**	**91**	**(15.6)**	**1**	**(3.7)**	**2**	**(28.6)**
Joint swelling	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Myalgia	6	(3.4)	19	(3.2)	0	(0.0)	1	(14.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**10**	**(5.6)**	**23**	**(3.9)**	**1**	**(3.7)**	**1**	**(14.3)**
Papilloma	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Thyroid neoplasm	0	(0.0)	0	(0.0)	1	(3.7)	0	(0.0)
Nervous system disorders	**46**	**(25.8)**	**122**	**(20.9)**	**7**	**(25.9)**	**1**	**(14.3)**
Dizziness	7	(3.9)	29	(5.0)	0	(0.0)	0	(0.0)
Headache	31	(17.4)	63	(10.8)	6	(22.2)	0	(0.0)
Hypoaesthesia	1	(0.6)	5	(0.9)	1	(3.7)	0	(0.0)
Paraesthesia	2	(1.1)	3	(0.5)	0	(0.0)	1	(14.3)
Psychiatric disorders	**28**	**(15.7)**	**82**	**(14.0)**	**3**	**(11.1)**	**1**	**(14.3)**
Abnormal dreams	1	(0.6)	18	(3.1)	2	(7.4)	1	(14.3)
Insomnia	9	(5.1)	22	(3.8)	2	(7.4)	1	(14.3)
Renal and urinary disorders	**5**	**(2.8)**	**13**	**(2.2)**	**1**	**(3.7)**	**0**	**(0.0)**
Pollakiuria	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**5**	**(4.0)**	**29**	**(7.6)**	**0**	**(0.0)**	**1**	**(16.7)**	**1**	**(1.9)**	**7**	**(3.4)**	**1**	**(12.5)**	**0**	**(0.0)**
Dysmenorrhoea	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)
Genital cyst	0	(0.0)	0	(0.0)	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**15**	**(11.9)**	**58**	**(15.3)**	**2**	**(10.5)**	**1**	**(16.7)**	**5**	**(9.6)**	**32**	**(15.6)**	**3**	**(37.5)**	**0**	**(0.0)**
Cough	4	(3.2)	22	(5.8)	1	(5.3)	1	(16.7)	1	(1.9)	12	(5.9)	1	(12.5)	0	(0.0)
Epistaxis	2	(1.6)	3	(0.8)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	0	(0.0)	0	(0.0)
Respiratory disorder	0	(0.0)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)
Rhinitis allergic	7	(5.6)	8	(2.1)	0	(0.0)	0	(0.0)	2	(3.8)	3	(1.5)	1	(12.5)	0	(0.0)
Rhinorrhoea	3	(2.4)	4	(1.1)	0	(0.0)	1	(16.7)	1	(1.9)	1	(0.5)	0	(0.0)	0	(0.0)
Skin and subcutaneous tissue disorders	**28**	**(22.2)**	**71**	**(18.7)**	**2**	**(10.5)**	**0**	**(0.0)**	**10**	**(19.2)**	**52**	**(25.4)**	**1**	**(12.5)**	**0**	**(0.0)**
Lipodystrophy acquired	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	1	(0.5)	1	(12.5)	0	(0.0)
Miliaria	0	(0.0)	0	(0.0)	1	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pruritus	6	(4.8)	9	(2.4)	0	(0.0)	0	(0.0)	2	(3.8)	13	(6.3)	0	(0.0)	0	(0.0)
Vascular disorders	**4**	**(3.2)**	**21**	**(5.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(9.6)**	**6**	**(2.9)**	**0**	**(0.0)**	**0**	**(0.0)**

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**6**	**(3.4)**	**36**	**(6.2)**	**1**	**(3.7)**	**1**	**(14.3)**
Dysmenorrhoea	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)
Genital cyst	0	(0.0)	0	(0.0)	0	(0.0)	1	(14.3)
Respiratory, thoracic and mediastinal disorders	**20**	**(11.2)**	**90**	**(15.4)**	**5**	**(18.5)**	**1**	**(14.3)**
Cough	5	(2.8)	34	(5.8)	2	(7.4)	1	(14.3)
Epistaxis	2	(1.1)	4	(0.7)	1	(3.7)	0	(0.0)
Respiratory disorder	0	(0.0)	1	(0.2)	1	(3.7)	0	(0.0)
Rhinitis allergic	9	(5.1)	11	(1.9)	1	(3.7)	0	(0.0)
Rhinorrhoea	4	(2.2)	5	(0.9)	0	(0.0)	1	(14.3)
Skin and subcutaneous tissue disorders	**38**	**(21.3)**	**123**	**(21.0)**	**3**	**(11.1)**	**0**	**(0.0)**
Lipodystrophy acquired	0	(0.0)	1	(0.2)	2	(7.4)	0	(0.0)
Miliaria	0	(0.0)	0	(0.0)	1	(3.7)	0	(0.0)
Pruritus	8	(4.5)	22	(3.8)	0	(0.0)	0	(0.0)
Vascular disorders	**9**	**(5.1)**	**27**	**(4.6)**	**0**	**(0.0)**	**0**	**(0.0)**

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U		Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	**4**	**(3.2)**	**21**	**(5.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(9.6)**	**6**	**(2.9)**	**0**	**(0.0)**	**0**	**(0.0)**
Hypertension	3	(2.4)	13	(3.4)	0	(0.0)	0	(0.0)	4	(7.7)	3	(1.5)	0	(0.0)	0	(0.0)

Subjects With Clinical Adverse Events by Ethnicity (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total							
	Hispanic Or Latino		Not Hispanic Or Latino		Not Reported		U	
	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	**9**	**(5.1)**	**27**	**(4.6)**	**0**	**(0.0)**	**0**	**(0.0)**
Hypertension	7	(3.9)	16	(2.7)	0	(0.0)	0	(0.0)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 49

Adverse Event Summary by Ethnicity
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD								Raltegravir 400 mg BID							
	Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown		Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	126		380		19		6		52		205		8		1	
with one or more adverse events	15	(11.9)	21	(5.5)	1	(5.3)	0	(0.0)	11	(21.2)	18	(8.8)	1	(12.5)	0	(0.0)
with no adverse event	111	(88.1)	359	(94.5)	18	(94.7)	6	(100.0)	41	(78.8)	187	(91.2)	7	(87.5)	1	(100.0)
with drug-related[†] adverse events	3	(2.4)	5	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	4	(2.0)	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	2	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	1	(0.8)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	1	(0.8)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Event Summary by Ethnicity
Laboratory Adverse Events
Weeks 0-48

	Total							
	Hispanic or Latino		Not Hispanic or Latino		Not Reported		Unknown	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	178		585		27		7	
with one or more adverse events	26	(14.6)	39	(6.7)	2	(7.4)	0	(0.0)
with no adverse event	152	(85.4)	546	(93.3)	25	(92.6)	7	(100.0)
with drug-related† adverse events	3	(1.7)	9	(1.5)	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	1	(0.6)	1	(0.2)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	1	(0.6)	1	(0.2)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 50

Adverse Event Summary by Race
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		83		98		46		0		301	
with one or more adverse events	2	(66.7)	58	(69.9)	89	(90.8)	41	(89.1)	0		249	(82.7)
with no adverse event	1	(33.3)	25	(30.1)	9	(9.2)	5	(10.9)	0		52	(17.3)
with drug-related[†] adverse events	1	(33.3)	13	(15.7)	27	(27.6)	11	(23.9)	0		78	(25.9)
with serious adverse events	0	(0.0)	4	(4.8)	11	(11.2)	1	(2.2)	0		15	(5.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
who died	0	(0.0)	0	(0.0)	1	(1.0)	1	(2.2)	0		0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	1	(1.0)	2	(4.3)	0		1	(0.3)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(1.0)	1	(2.2)	0		1	(0.3)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)

Adverse Event Summary by Race
Clinical Adverse Events
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		40		36		14		1		172	
with one or more adverse events	3	(100.0)	34	(85.0)	34	(94.4)	11	(78.6)	1	(100.0)	148	(86.0)
with no adverse event	0	(0.0)	6	(15.0)	2	(5.6)	3	(21.4)	0	(0.0)	24	(14.0)
with drug-related[†] adverse events	1	(33.3)	10	(25.0)	13	(36.1)	4	(28.6)	1	(100.0)	39	(22.7)
with serious adverse events	0	(0.0)	5	(12.5)	3	(8.3)	0	(0.0)	0	(0.0)	17	(9.9)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(2.8)	0	(0.0)	0	(0.0)	1	(0.6)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
discontinued[‡] due to an adverse event	0	(0.0)	1	(2.5)	2	(5.6)	1	(7.1)	0	(0.0)	2	(1.2)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(2.8)	1	(7.1)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Event Summary by Race
Clinical Adverse Events
Weeks 0-48

	Total											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	6		123		134		60		1		473	
with one or more adverse events	5	(83.3)	92	(74.8)	123	(91.8)	52	(86.7)	1	(100.0)	397	(83.9)
with no adverse event	1	(16.7)	31	(25.2)	11	(8.2)	8	(13.3)	0	(0.0)	76	(16.1)
with drug-related[†] adverse events	2	(33.3)	23	(18.7)	40	(29.9)	15	(25.0)	1	(100.0)	117	(24.7)
with serious adverse events	0	(0.0)	9	(7.3)	14	(10.4)	1	(1.7)	0	(0.0)	32	(6.8)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)	0	(0.0)	2	(0.4)
who died	0	(0.0)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	1	(0.2)
discontinued[‡] due to an adverse event	0	(0.0)	1	(0.8)	3	(2.2)	3	(5.0)	0	(0.0)	3	(0.6)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	1	(0.8)	1	(0.7)	1	(1.7)	0	(0.0)	2	(0.4)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 51

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		83		98		46		0		301	
with one or more adverse events	2	(66.7)	58	(69.9)	89	(90.8)	41	(89.1)	0		249	(82.7)
with no adverse events	1	(33.3)	25	(30.1)	9	(9.2)	5	(10.9)	0		52	(17.3)
Blood and lymphatic system disorders	**0**	**(0.0)**	**2**	**(2.4)**	**6**	**(6.1)**	**2**	**(4.3)**	**0**		**14**	**(4.7)**
Lymphadenopathy	0	(0.0)	2	(2.4)	5	(5.1)	1	(2.2)	0		7	(2.3)
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Ear and labyrinth disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(2.0)**	**2**	**(4.3)**	**0**		**10**	**(3.3)**
Eye disorders	**0**	**(0.0)**	**3**	**(3.6)**	**7**	**(7.1)**	**2**	**(4.3)**	**0**		**5**	**(1.7)**
Conjunctival haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Keratitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Gastrointestinal disorders	**2**	**(66.7)**	**22**	**(26.5)**	**47**	**(48.0)**	**24**	**(52.2)**	**0**		**114**	**(37.9)**
Abdominal distension	1	(33.3)	0	(0.0)	0	(0.0)	1	(2.2)	0		8	(2.7)
Abdominal hernia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Abdominal pain	0	(0.0)	2	(2.4)	8	(8.2)	5	(10.9)	0		25	(8.3)
Diarrhoea	1	(33.3)	7	(8.4)	9	(9.2)	12	(26.1)	0		29	(9.6)
Dyspepsia	1	(33.3)	2	(2.4)	3	(3.1)	2	(4.3)	0		4	(1.3)
Flatulence	0	(0.0)	0	(0.0)	3	(3.1)	1	(2.2)	0		1	(0.3)
Food poisoning	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Haemorrhoids	1	(33.3)	2	(2.4)	1	(1.0)	0	(0.0)	0		2	(0.7)
Mouth ulceration	0	(0.0)	1	(1.2)	0	(0.0)	0	(0.0)	0		0	(0.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		40		36		14		1		172	
with one or more adverse events	3	(100.0)	34	(85.0)	34	(94.4)	11	(78.6)	1	(100.0)	148	(86.0)
with no adverse events	0	(0.0)	6	(15.0)	2	(5.6)	3	(21.4)	0	(0.0)	24	(14.0)
Blood and lymphatic system disorders	**0**	**(0.0)**	**2**	**(5.0)**	**0**	**(0.0)**	**1**	**(7.1)**	**0**	**(0.0)**	**5**	**(2.9)**
Lymphadenopathy	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(1.7)
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Ear and labyrinth disorders	**0**	**(0.0)**	**2**	**(5.0)**	**1**	**(2.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(2.9)**
Eye disorders	**1**	**(33.3)**	**3**	**(7.5)**	**1**	**(2.8)**	**1**	**(7.1)**	**0**	**(0.0)**	**3**	**(1.7)**
Conjunctival haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Keratitis	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**0**	**(0.0)**	**16**	**(40.0)**	**16**	**(44.4)**	**4**	**(28.6)**	**1**	**(100.0)**	**62**	**(36.0)**
Abdominal distension	0	(0.0)	3	(7.5)	0	(0.0)	0	(0.0)	0	(0.0)	5	(2.9)
Abdominal hernia	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Abdominal pain	0	(0.0)	0	(0.0)	3	(8.3)	1	(7.1)	0	(0.0)	7	(4.1)
Diarrhoea	0	(0.0)	5	(12.5)	7	(19.4)	0	(0.0)	0	(0.0)	18	(10.5)
Dyspepsia	0	(0.0)	0	(0.0)	2	(5.6)	0	(0.0)	0	(0.0)	5	(2.9)
Flatulence	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	8	(4.7)
Food poisoning	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1	(0.6)
Haemorrhoids	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(1.7)
Mouth ulceration	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	0	(0.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	6		123		134		60		1		473	
with one or more adverse events	5	(83.3)	92	(74.8)	123	(91.8)	52	(86.7)	1	(100.0)	397	(83.9)
with no adverse events	1	(16.7)	31	(25.2)	11	(8.2)	8	(13.3)	0	(0.0)	76	(16.1)
Blood and lymphatic system disorders	**0**	**(0.0)**	**4**	**(3.3)**	**6**	**(4.5)**	**3**	**(5.0)**	**0**	**(0.0)**	**19**	**(4.0)**
Lymphadenopathy	0	(0.0)	4	(3.3)	5	(3.7)	1	(1.7)	0	(0.0)	10	(2.1)
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	1	(0.2)
Ear and labyrinth disorders	**0**	**(0.0)**	**2**	**(1.6)**	**3**	**(2.2)**	**2**	**(3.3)**	**0**	**(0.0)**	**15**	**(3.2)**
Eye disorders	**1**	**(16.7)**	**6**	**(4.9)**	**8**	**(6.0)**	**3**	**(5.0)**	**0**	**(0.0)**	**8**	**(1.7)**
Conjunctival haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)
Keratitis	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**2**	**(33.3)**	**38**	**(30.9)**	**63**	**(47.0)**	**28**	**(46.7)**	**1**	**(100.0)**	**176**	**(37.2)**
Abdominal distension	1	(16.7)	3	(2.4)	0	(0.0)	1	(1.7)	0	(0.0)	13	(2.7)
Abdominal hernia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	1	(0.2)
Abdominal pain	0	(0.0)	2	(1.6)	11	(8.2)	6	(10.0)	0	(0.0)	32	(6.8)
Diarrhoea	1	(16.7)	12	(9.8)	16	(11.9)	12	(20.0)	0	(0.0)	47	(9.9)
Dyspepsia	1	(16.7)	2	(1.6)	5	(3.7)	2	(3.3)	0	(0.0)	9	(1.9)
Flatulence	0	(0.0)	0	(0.0)	3	(2.2)	2	(3.3)	0	(0.0)	9	(1.9)
Food poisoning	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(100.0)	1	(0.2)
Haemorrhoids	1	(16.7)	2	(1.6)	1	(0.7)	0	(0.0)	0	(0.0)	5	(1.1)
Mouth ulceration	0	(0.0)	1	(0.8)	0	(0.0)	0	(0.0)	1	(100.0)	0	(0.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**2**	**(66.7)**	**22**	**(26.5)**	**47**	**(48.0)**	**24**	**(52.2)**	**0**		**114**	**(37.9)**
Nausea	1	(33.3)	4	(4.8)	15	(15.3)	3	(6.5)	0		37	(12.3)
Proctitis	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0		4	(1.3)
Vomiting	0	(0.0)	4	(4.8)	12	(12.2)	3	(6.5)	0		16	(5.3)
General disorders and administration site conditions	**1**	**(33.3)**	**12**	**(14.5)**	**19**	**(19.4)**	**3**	**(6.5)**	**0**		**49**	**(16.3)**
Fatigue	0	(0.0)	3	(3.6)	9	(9.2)	1	(2.2)	0		20	(6.6)
Feeling hot	1	(33.3)	0	(0.0)	0	(0.0)	1	(2.2)	0		0	(0.0)
Influenza like illness	0	(0.0)	4	(4.8)	1	(1.0)	0	(0.0)	0		4	(1.3)
Pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Pyrexia	0	(0.0)	5	(6.0)	1	(1.0)	0	(0.0)	0		15	(5.0)
Thirst	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Xerosis	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Infections and infestations	**1**	**(33.3)**	**26**	**(31.3)**	**57**	**(58.2)**	**30**	**(65.2)**	**0**		**157**	**(52.2)**
Bronchitis	0	(0.0)	0	(0.0)	6	(6.1)	3	(6.5)	0		8	(2.7)
Cellulitis	0	(0.0)	1	(1.2)	0	(0.0)	0	(0.0)	0		3	(1.0)
Chikungunya virus infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	0		1	(0.3)
Chlamydial infection	0	(0.0)	0	(0.0)	0	(0.0)	3	(6.5)	0		1	(0.3)
Conjunctivitis	0	(0.0)	0	(0.0)	0	(0.0)	2	(4.3)	0		4	(1.3)
Gastroenteritis	0	(0.0)	2	(2.4)	5	(5.1)	1	(2.2)	0		8	(2.7)
Genital herpes simplex	0	(0.0)	1	(1.2)	1	(1.0)	0	(0.0)	0		0	(0.0)
Helicobacter infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**0**	**(0.0)**	**16**	**(40.0)**	**16**	**(44.4)**	**4**	**(28.6)**	**1**	**(100.0)**	**62**	**(36.0)**
Nausea	0	(0.0)	3	(7.5)	2	(5.6)	2	(14.3)	1	(100.0)	18	(10.5)
Proctitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	3	(1.7)
Vomiting	0	(0.0)	3	(7.5)	3	(8.3)	0	(0.0)	0	(0.0)	9	(5.2)
General disorders and administration site conditions	**0**	**(0.0)**	**10**	**(25.0)**	**7**	**(19.4)**	**0**	**(0.0)**	**1**	**(100.0)**	**31**	**(18.0)**
Fatigue	0	(0.0)	2	(5.0)	4	(11.1)	0	(0.0)	1	(100.0)	9	(5.2)
Feeling hot	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Influenza like illness	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	9	(5.2)
Pain	0	(0.0)	0	(0.0)	1	(2.8)	0	(0.0)	1	(100.0)	0	(0.0)
Pyrexia	0	(0.0)	4	(10.0)	0	(0.0)	0	(0.0)	0	(0.0)	7	(4.1)
Thirst	0	(0.0)	0	(0.0)	2	(5.6)	0	(0.0)	0	(0.0)	1	(0.6)
Xerosis	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infections and infestations	**2**	**(66.7)**	**15**	**(37.5)**	**19**	**(52.8)**	**9**	**(64.3)**	**1**	**(100.0)**	**104**	**(60.5)**
Bronchitis	0	(0.0)	0	(0.0)	1	(2.8)	2	(14.3)	0	(0.0)	7	(4.1)
Cellulitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	3	(1.7)
Chikungunya virus infection	0	(0.0)	0	(0.0)	1	(2.8)	1	(7.1)	0	(0.0)	0	(0.0)
Chlamydial infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	5	(2.9)
Conjunctivitis	1	(33.3)	0	(0.0)	1	(2.8)	0	(0.0)	0	(0.0)	2	(1.2)
Gastroenteritis	0	(0.0)	2	(5.0)	0	(0.0)	1	(7.1)	0	(0.0)	8	(4.7)
Genital herpes simplex	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	1	(0.6)
Helicobacter infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**2**	**(33.3)**	**38**	**(30.9)**	**63**	**(47.0)**	**28**	**(46.7)**	**1**	**(100.0)**	**176**	**(37.2)**
Nausea	1	(16.7)	7	(5.7)	17	(12.7)	5	(8.3)	1	(100.0)	55	(11.6)
Proctitis	0	(0.0)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	7	(1.5)
Vomiting	0	(0.0)	7	(5.7)	15	(11.2)	3	(5.0)	0	(0.0)	25	(5.3)
General disorders and administration site conditions	**1**	**(16.7)**	**22**	**(17.9)**	**26**	**(19.4)**	**3**	**(5.0)**	**1**	**(100.0)**	**80**	**(16.9)**
Fatigue	0	(0.0)	5	(4.1)	13	(9.7)	1	(1.7)	1	(100.0)	29	(6.1)
Feeling hot	1	(16.7)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)
Influenza like illness	0	(0.0)	6	(4.9)	1	(0.7)	0	(0.0)	0	(0.0)	13	(2.7)
Pain	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)	1	(100.0)	1	(0.2)
Pyrexia	0	(0.0)	9	(7.3)	1	(0.7)	0	(0.0)	0	(0.0)	22	(4.7)
Thirst	0	(0.0)	0	(0.0)	2	(1.5)	0	(0.0)	0	(0.0)	2	(0.4)
Xerosis	1	(16.7)	1	(0.8)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infections and infestations	**3**	**(50.0)**	**41**	**(33.3)**	**76**	**(56.7)**	**39**	**(65.0)**	**1**	**(100.0)**	**261**	**(55.2)**
Bronchitis	0	(0.0)	0	(0.0)	7	(5.2)	5	(8.3)	0	(0.0)	15	(3.2)
Cellulitis	0	(0.0)	1	(0.8)	0	(0.0)	1	(1.7)	0	(0.0)	6	(1.3)
Chikungunya virus infection	0	(0.0)	0	(0.0)	1	(0.7)	2	(3.3)	0	(0.0)	1	(0.2)
Chlamydial infection	0	(0.0)	0	(0.0)	0	(0.0)	3	(5.0)	0	(0.0)	6	(1.3)
Conjunctivitis	1	(16.7)	0	(0.0)	1	(0.7)	2	(3.3)	0	(0.0)	6	(1.3)
Gastroenteritis	0	(0.0)	4	(3.3)	5	(3.7)	2	(3.3)	0	(0.0)	16	(3.4)
Genital herpes simplex	0	(0.0)	1	(0.8)	1	(0.7)	1	(1.7)	0	(0.0)	1	(0.2)
Helicobacter infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	1	(0.2)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**1**	**(33.3)**	**26**	**(31.3)**	**57**	**(58.2)**	**30**	**(65.2)**	**0**		**157**	**(52.2)**
Herpes zoster	0	(0.0)	1	(1.2)	1	(1.0)	2	(4.3)	0		6	(2.0)
Influenza	0	(0.0)	1	(1.2)	2	(2.0)	7	(15.2)	0		8	(2.7)
Latent syphilis	0	(0.0)	1	(1.2)	0	(0.0)	0	(0.0)	0		1	(0.3)
Nasopharyngitis	0	(0.0)	5	(6.0)	3	(3.1)	2	(4.3)	0		34	(11.3)
Onychomycosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.2)	0		4	(1.3)
Oral herpes	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0		7	(2.3)
Pharyngitis	0	(0.0)	2	(2.4)	2	(2.0)	3	(6.5)	0		7	(2.3)
Pharyngotonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	5	(5.1)	0	(0.0)	0		4	(1.3)
Sinusitis	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0		5	(1.7)
Syphilis	0	(0.0)	3	(3.6)	1	(1.0)	0	(0.0)	0		10	(3.3)
Tonsillitis	0	(0.0)	0	(0.0)	3	(3.1)	4	(8.7)	0		6	(2.0)
Upper respiratory tract infection	0	(0.0)	7	(8.4)	13	(13.3)	1	(2.2)	0		19	(6.3)
Urethritis	0	(0.0)	0	(0.0)	2	(2.0)	1	(2.2)	0		6	(2.0)
Urethritis gonococcal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		2	(0.7)
Viral infection	1	(33.3)	0	(0.0)	2	(2.0)	0	(0.0)	0		1	(0.3)
Vulvovaginal candidiasis	0	(0.0)	0	(0.0)	5	(5.1)	0	(0.0)	0		0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**11**	**(13.3)**	**9**	**(9.2)**	**4**	**(8.7)**	**0**		**33**	**(11.0)**
Accidental overdose	0	(0.0)	6	(7.2)	1	(1.0)	0	(0.0)	0		15	(5.0)
Investigations	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(5.1)**	**0**	**(0.0)**	**0**		**7**	**(2.3)**

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**2**	**(66.7)**	**15**	**(37.5)**	**19**	**(52.8)**	**9**	**(64.3)**	**1**	**(100.0)**	**104**	**(60.5)**
Herpes zoster	0	(0.0)	0	(0.0)	1	(2.8)	1	(7.1)	0	(0.0)	1	(0.6)
Influenza	0	(0.0)	2	(5.0)	1	(2.8)	3	(21.4)	0	(0.0)	6	(3.5)
Latent syphilis	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nasopharyngitis	0	(0.0)	2	(5.0)	2	(5.6)	1	(7.1)	0	(0.0)	17	(9.9)
Onychomycosis	1	(33.3)	0	(0.0)	1	(2.8)	0	(0.0)	0	(0.0)	0	(0.0)
Oral herpes	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	2	(1.2)
Pharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	8	(4.7)
Pharyngotonsillitis	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	5	(2.9)
Sinusitis	0	(0.0)	0	(0.0)	2	(5.6)	0	(0.0)	0	(0.0)	3	(1.7)
Syphilis	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	12	(7.0)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	6	(3.5)
Upper respiratory tract infection	0	(0.0)	0	(0.0)	4	(11.1)	2	(14.3)	1	(100.0)	12	(7.0)
Urethritis	0	(0.0)	0	(0.0)	1	(2.8)	1	(7.1)	0	(0.0)	5	(2.9)
Urethritis gonococcal	0	(0.0)	0	(0.0)	1	(2.8)	1	(7.1)	0	(0.0)	0	(0.0)
Viral infection	1	(33.3)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Vulvovaginal candidiasis	0	(0.0)	0	(0.0)	1	(2.8)	0	(0.0)	0	(0.0)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**5**	**(12.5)**	**4**	**(11.1)**	**1**	**(7.1)**	**0**	**(0.0)**	**18**	**(10.5)**
Accidental overdose	0	(0.0)	3	(7.5)	1	(2.8)	1	(7.1)	0	(0.0)	5	(2.9)
Investigations	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(2.9)**

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**3**	**(50.0)**	**41**	**(33.3)**	**76**	**(56.7)**	**39**	**(65.0)**	**1**	**(100.0)**	**261**	**(55.2)**
Herpes zoster	0	(0.0)	1	(0.8)	2	(1.5)	3	(5.0)	0	(0.0)	7	(1.5)
Influenza	0	(0.0)	3	(2.4)	3	(2.2)	10	(16.7)	0	(0.0)	14	(3.0)
Latent syphilis	0	(0.0)	3	(2.4)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nasopharyngitis	0	(0.0)	7	(5.7)	5	(3.7)	3	(5.0)	0	(0.0)	51	(10.8)
Onychomycosis	1	(16.7)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	4	(0.8)
Oral herpes	0	(0.0)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	9	(1.9)
Pharyngitis	0	(0.0)	2	(1.6)	2	(1.5)	3	(5.0)	0	(0.0)	15	(3.2)
Pharyngotonsillitis	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	5	(3.7)	0	(0.0)	0	(0.0)	9	(1.9)
Sinusitis	0	(0.0)	0	(0.0)	3	(2.2)	0	(0.0)	0	(0.0)	8	(1.7)
Syphilis	0	(0.0)	5	(4.1)	1	(0.7)	0	(0.0)	0	(0.0)	22	(4.7)
Tonsillitis	0	(0.0)	0	(0.0)	3	(2.2)	4	(6.7)	0	(0.0)	12	(2.5)
Upper respiratory tract infection	0	(0.0)	7	(5.7)	17	(12.7)	3	(5.0)	1	(100.0)	31	(6.6)
Urethritis	0	(0.0)	0	(0.0)	3	(2.2)	2	(3.3)	0	(0.0)	11	(2.3)
Urethritis gonococcal	0	(0.0)	0	(0.0)	1	(0.7)	1	(1.7)	0	(0.0)	2	(0.4)
Viral infection	2	(33.3)	1	(0.8)	2	(1.5)	0	(0.0)	0	(0.0)	2	(0.4)
Vulvovaginal candidiasis	0	(0.0)	0	(0.0)	6	(4.5)	0	(0.0)	0	(0.0)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**16**	**(13.0)**	**13**	**(9.7)**	**5**	**(8.3)**	**0**	**(0.0)**	**51**	**(10.8)**
Accidental overdose	0	(0.0)	9	(7.3)	2	(1.5)	1	(1.7)	0	(0.0)	20	(4.2)
Investigations	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(3.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**12**	**(2.5)**

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**0**	**(0.0)**	**2**	**(2.4)**	**7**	**(7.1)**	**1**	**(2.2)**	**0**		**17**	**(5.6)**
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Musculoskeletal and connective tissue disorders	**1**	**(33.3)**	**7**	**(8.4)**	**20**	**(20.4)**	**7**	**(15.2)**	**0**		**54**	**(17.9)**
Arthralgia	0	(0.0)	0	(0.0)	6	(6.1)	1	(2.2)	0		9	(3.0)
Back pain	0	(0.0)	2	(2.4)	4	(4.1)	2	(4.3)	0		16	(5.3)
Muscle spasms	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Myalgia	0	(0.0)	2	(2.4)	5	(5.1)	0	(0.0)	0		12	(4.0)
Neck pain	0	(0.0)	1	(1.2)	1	(1.0)	0	(0.0)	0		5	(1.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(33.3)**	**4**	**(4.8)**	**3**	**(3.1)**	**2**	**(4.3)**	**0**		**15**	**(5.0)**
Anogenital warts	1	(33.3)	3	(3.6)	1	(1.0)	1	(2.2)	0		10	(3.3)
Melanocytic naevus	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Nervous system disorders	**1**	**(33.3)**	**14**	**(16.9)**	**24**	**(24.5)**	**12**	**(26.1)**	**0**		**71**	**(23.6)**
Dizziness	1	(33.3)	5	(6.0)	5	(5.1)	1	(2.2)	0		12	(4.0)
Dysgeusia	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Headache	1	(33.3)	7	(8.4)	14	(14.3)	10	(21.7)	0		39	(13.0)
Hypoaesthesia	0	(0.0)	1	(1.2)	1	(1.0)	0	(0.0)	0		0	(0.0)
Syncope	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		4	(1.3)
Psychiatric disorders	**0**	**(0.0)**	**9**	**(10.8)**	**7**	**(7.1)**	**6**	**(13.0)**	**0**		**49**	**(16.3)**
Abnormal dreams	0	(0.0)	4	(4.8)	1	(1.0)	0	(0.0)	0		10	(3.3)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**0**	**(0.0)**	**2**	**(5.0)**	**3**	**(8.3)**	**1**	**(7.1)**	**0**	**(0.0)**	**7**	**(4.1)**
Hypertriglyceridaemia	0	(0.0)	1	(2.5)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**4**	**(10.0)**	**3**	**(8.3)**	**1**	**(7.1)**	**1**	**(100.0)**	**27**	**(15.7)**
Arthralgia	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	1	(100.0)	4	(2.3)
Back pain	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	7	(4.1)
Muscle spasms	0	(0.0)	0	(0.0)	1	(2.8)	0	(0.0)	0	(0.0)	1	(0.6)
Myalgia	0	(0.0)	1	(2.5)	1	(2.8)	0	(0.0)	0	(0.0)	5	(2.9)
Neck pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	1	(0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(2.8)**	**1**	**(7.1)**	**0**	**(0.0)**	**8**	**(4.7)**
Anogenital warts	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.2)
Melanocytic naevus	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Nervous system disorders	**2**	**(66.7)**	**11**	**(27.5)**	**4**	**(11.1)**	**2**	**(14.3)**	**1**	**(100.0)**	**34**	**(19.8)**
Dizziness	1	(33.3)	5	(12.5)	1	(2.8)	0	(0.0)	0	(0.0)	5	(2.9)
Dysgeusia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Headache	1	(33.3)	4	(10.0)	2	(5.6)	2	(14.3)	1	(100.0)	19	(11.0)
Hypoaesthesia	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(1.7)
Syncope	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.2)
Psychiatric disorders	**1**	**(33.3)**	**6**	**(15.0)**	**1**	**(2.8)**	**1**	**(7.1)**	**0**	**(0.0)**	**34**	**(19.8)**
Abnormal dreams	0	(0.0)	2	(5.0)	0	(0.0)	1	(7.1)	0	(0.0)	4	(2.3)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**0**	**(0.0)**	**4**	**(3.3)**	**10**	**(7.5)**	**2**	**(3.3)**	**0**	**(0.0)**	**24**	**(5.1)**
Hypertriglyceridaemia	0	(0.0)	1	(0.8)	0	(0.0)	1	(1.7)	0	(0.0)	1	(0.2)
Musculoskeletal and connective tissue disorders	**1**	**(16.7)**	**11**	**(8.9)**	**23**	**(17.2)**	**8**	**(13.3)**	**1**	**(100.0)**	**81**	**(17.1)**
Arthralgia	0	(0.0)	1	(0.8)	6	(4.5)	1	(1.7)	1	(100.0)	13	(2.7)
Back pain	0	(0.0)	3	(2.4)	4	(3.0)	2	(3.3)	0	(0.0)	23	(4.9)
Muscle spasms	1	(16.7)	0	(0.0)	1	(0.7)	0	(0.0)	0	(0.0)	1	(0.2)
Myalgia	0	(0.0)	3	(2.4)	6	(4.5)	0	(0.0)	0	(0.0)	17	(3.6)
Neck pain	0	(0.0)	1	(0.8)	1	(0.7)	1	(1.7)	0	(0.0)	6	(1.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(16.7)**	**4**	**(3.3)**	**4**	**(3.0)**	**3**	**(5.0)**	**0**	**(0.0)**	**23**	**(4.9)**
Anogenital warts	1	(16.7)	3	(2.4)	1	(0.7)	1	(1.7)	0	(0.0)	12	(2.5)
Melanocytic naevus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)
Nervous system disorders	**3**	**(50.0)**	**25**	**(20.3)**	**28**	**(20.9)**	**14**	**(23.3)**	**1**	**(100.0)**	**105**	**(22.2)**
Dizziness	2	(33.3)	10	(8.1)	6	(4.5)	1	(1.7)	0	(0.0)	17	(3.6)
Dysgeusia	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Headache	2	(33.3)	11	(8.9)	16	(11.9)	12	(20.0)	1	(100.0)	58	(12.3)
Hypoaesthesia	0	(0.0)	3	(2.4)	1	(0.7)	0	(0.0)	0	(0.0)	3	(0.6)
Syncope	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	6	(1.3)
Psychiatric disorders	**1**	**(16.7)**	**15**	**(12.2)**	**8**	**(6.0)**	**7**	**(11.7)**	**0**	**(0.0)**	**83**	**(17.5)**
Abnormal dreams	0	(0.0)	6	(4.9)	1	(0.7)	1	(1.7)	0	(0.0)	14	(3.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**0**	**(0.0)**	**9**	**(10.8)**	**7**	**(7.1)**	**6**	**(13.0)**	**0**		**49**	**(16.3)**
Depression	0	(0.0)	0	(0.0)	3	(3.1)	2	(4.3)	0		9	(3.0)
Insomnia	0	(0.0)	4	(4.8)	1	(1.0)	0	(0.0)	0		16	(5.3)
Renal and urinary disorders	**0**	**(0.0)**	**1**	**(1.2)**	**3**	**(3.1)**	**1**	**(2.2)**	**0**		**8**	**(2.7)**
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(1.2)**	**19**	**(19.4)**	**0**	**(0.0)**	**0**		**15**	**(5.0)**
Cervical dysplasia	0	(0.0)	0	(0.0)	5	(5.1)	0	(0.0)	0		0	(0.0)
Vaginal discharge	0	(0.0)	0	(0.0)	5	(5.1)	0	(0.0)	0		0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**10**	**(12.0)**	**16**	**(16.3)**	**6**	**(13.0)**	**0**		**44**	**(14.6)**
Cough	0	(0.0)	3	(3.6)	8	(8.2)	2	(4.3)	0		15	(5.0)
Nasal congestion	0	(0.0)	1	(1.2)	3	(3.1)	0	(0.0)	0		2	(0.7)
Oropharyngeal pain	0	(0.0)	2	(2.4)	6	(6.1)	1	(2.2)	0		11	(3.7)
Rhinitis allergic	0	(0.0)	2	(2.4)	3	(3.1)	3	(6.5)	0		7	(2.3)
Sinus congestion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		5	(1.7)
Skin and subcutaneous tissue disorders	**1**	**(33.3)**	**12**	**(14.5)**	**19**	**(19.4)**	**10**	**(21.7)**	**0**		**59**	**(19.6)**
Acne	0	(0.0)	1	(1.2)	2	(2.0)	0	(0.0)	0		7	(2.3)
Ecchymosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		1	(0.3)
Macule	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Papule	0	(0.0)	0	(0.0)	2	(2.0)	0	(0.0)	0		1	(0.3)
Pruritus	1	(33.3)	1	(1.2)	5	(5.1)	3	(6.5)	0		5	(1.7)
Rash	1	(33.3)	1	(1.2)	8	(8.2)	1	(2.2)	0		12	(4.0)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**1**	**(33.3)**	**6**	**(15.0)**	**1**	**(2.8)**	**1**	**(7.1)**	**0**	**(0.0)**	**34**	**(19.8)**
Depression	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	10	(5.8)
Insomnia	1	(33.3)	2	(5.0)	1	(2.8)	0	(0.0)	0	(0.0)	9	(5.2)
Renal and urinary disorders	**0**	**(0.0)**	**1**	**(2.5)**	**2**	**(5.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(1.7)**
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(2.5)**	**1**	**(2.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**7**	**(4.1)**
Cervical dysplasia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.6)
Vaginal discharge	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**9**	**(22.5)**	**6**	**(16.7)**	**2**	**(14.3)**	**0**	**(0.0)**	**23**	**(13.4)**
Cough	0	(0.0)	4	(10.0)	0	(0.0)	0	(0.0)	0	(0.0)	10	(5.8)
Nasal congestion	0	(0.0)	2	(5.0)	0	(0.0)	0	(0.0)	0	(0.0)	4	(2.3)
Oropharyngeal pain	0	(0.0)	2	(5.0)	3	(8.3)	1	(7.1)	0	(0.0)	3	(1.7)
Rhinitis allergic	0	(0.0)	1	(2.5)	1	(2.8)	1	(7.1)	0	(0.0)	3	(1.7)
Sinus congestion	0	(0.0)	0	(0.0)	2	(5.6)	0	(0.0)	0	(0.0)	1	(0.6)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**10**	**(25.0)**	**13**	**(36.1)**	**4**	**(28.6)**	**0**	**(0.0)**	**36**	**(20.9)**
Acne	0	(0.0)	1	(2.5)	0	(0.0)	1	(7.1)	0	(0.0)	1	(0.6)
Ecchymosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Macule	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Papule	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Pruritus	0	(0.0)	4	(10.0)	2	(5.6)	0	(0.0)	0	(0.0)	9	(5.2)
Rash	0	(0.0)	0	(0.0)	2	(5.6)	0	(0.0)	0	(0.0)	9	(5.2)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**1**	**(16.7)**	**15**	**(12.2)**	**8**	**(6.0)**	**7**	**(11.7)**	**0**	**(0.0)**	**83**	**(17.5)**
Depression	0	(0.0)	1	(0.8)	3	(2.2)	2	(3.3)	0	(0.0)	19	(4.0)
Insomnia	1	(16.7)	6	(4.9)	2	(1.5)	0	(0.0)	0	(0.0)	25	(5.3)
Renal and urinary disorders	**0**	**(0.0)**	**2**	**(1.6)**	**5**	**(3.7)**	**1**	**(1.7)**	**0**	**(0.0)**	**11**	**(2.3)**
Reproductive system and breast disorders	**0**	**(0.0)**	**2**	**(1.6)**	**20**	**(14.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**22**	**(4.7)**
Cervical dysplasia	0	(0.0)	0	(0.0)	5	(3.7)	0	(0.0)	0	(0.0)	1	(0.2)
Vaginal discharge	0	(0.0)	0	(0.0)	5	(3.7)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**19**	**(15.4)**	**22**	**(16.4)**	**8**	**(13.3)**	**0**	**(0.0)**	**67**	**(14.2)**
Cough	0	(0.0)	7	(5.7)	8	(6.0)	2	(3.3)	0	(0.0)	25	(5.3)
Nasal congestion	0	(0.0)	3	(2.4)	3	(2.2)	0	(0.0)	0	(0.0)	6	(1.3)
Oropharyngeal pain	0	(0.0)	4	(3.3)	9	(6.7)	2	(3.3)	0	(0.0)	14	(3.0)
Rhinitis allergic	0	(0.0)	3	(2.4)	4	(3.0)	4	(6.7)	0	(0.0)	10	(2.1)
Sinus congestion	0	(0.0)	0	(0.0)	2	(1.5)	0	(0.0)	0	(0.0)	6	(1.3)
Skin and subcutaneous tissue disorders	**1**	**(16.7)**	**22**	**(17.9)**	**32**	**(23.9)**	**14**	**(23.3)**	**0**	**(0.0)**	**95**	**(20.1)**
Acne	0	(0.0)	2	(1.6)	2	(1.5)	1	(1.7)	0	(0.0)	8	(1.7)
Ecchymosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	1	(0.2)
Macule	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)
Papule	0	(0.0)	0	(0.0)	2	(1.5)	1	(1.7)	0	(0.0)	1	(0.2)
Pruritus	1	(16.7)	5	(4.1)	7	(5.2)	3	(5.0)	0	(0.0)	14	(3.0)
Rash	1	(16.7)	1	(0.8)	10	(7.5)	1	(1.7)	0	(0.0)	21	(4.4)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(33.3)**	**12**	**(14.5)**	**19**	**(19.4)**	**10**	**(21.7)**	**0**		**59**	**(19.6)**
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
Rash maculo-papular	1	(33.3)	1	(1.2)	0	(0.0)	0	(0.0)	0		0	(0.0)
Rash papular	0	(0.0)	0	(0.0)	6	(6.1)	0	(0.0)	0		2	(0.7)
Vascular disorders	**0**	**(0.0)**	**1**	**(1.2)**	**6**	**(6.1)**	**1**	**(2.2)**	**0**		**17**	**(5.6)**
Hypertension	0	(0.0)	1	(1.2)	4	(4.1)	0	(0.0)	0		11	(3.7)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**10**	**(25.0)**	**13**	**(36.1)**	**4**	**(28.6)**	**0**	**(0.0)**	**36**	**(20.9)**
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.1)	0	(0.0)	0	(0.0)
Rash maculo-papular	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rash papular	0	(0.0)	0	(0.0)	3	(8.3)	0	(0.0)	0	(0.0)	1	(0.6)
Vascular disorders	**0**	**(0.0)**	**1**	**(2.5)**	**0**	**(0.0)**	**1**	**(7.1)**	**0**	**(0.0)**	**9**	**(5.2)**
Hypertension	0	(0.0)	1	(2.5)	0	(0.0)	1	(7.1)	0	(0.0)	5	(2.9)

Subjects With Clinical Adverse Events by Race (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Total											
	American Indian Or Alaska Native		Asian		Black Or African American		Multiple		Native Hawaiian Or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(16.7)**	**22**	**(17.9)**	**32**	**(23.9)**	**14**	**(23.3)**	**0**	**(0.0)**	**95**	**(20.1)**
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.7)	0	(0.0)	0	(0.0)
Rash maculo-papular	1	(16.7)	1	(0.8)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rash papular	0	(0.0)	0	(0.0)	9	(6.7)	0	(0.0)	0	(0.0)	3	(0.6)
Vascular disorders	**0**	**(0.0)**	**2**	**(1.6)**	**6**	**(4.5)**	**2**	**(3.3)**	**0**	**(0.0)**	**26**	**(5.5)**
Hypertension	0	(0.0)	2	(1.6)	4	(3.0)	1	(1.7)	0	(0.0)	16	(3.4)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 52

Adverse Event Summary by Race
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		83		98		46		0		301	
with one or more adverse events	2	(66.7)	5	(6.0)	4	(4.1)	7	(15.2)	0		19	(6.3)
with no adverse event	1	(33.3)	78	(94.0)	94	(95.9)	39	(84.8)	0		282	(93.7)
with drug-related[†] adverse events	0	(0.0)	0	(0.0)	2	(2.0)	0	(0.0)	0		6	(2.0)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		2	(0.7)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0		1	(0.3)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(1.0)	0	(0.0)	0		1	(0.3)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0		0	(0.0)

Adverse Event Summary by Race
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 400 mg BID											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	3		40		36		14		1		172	
with one or more adverse events	0	(0.0)	2	(5.0)	2	(5.6)	3	(21.4)	0	(0.0)	23	(13.4)
with no adverse event	3	(100.0)	38	(95.0)	34	(94.4)	11	(78.6)	1	(100.0)	149	(86.6)
with drug-related[†] adverse events	0	(0.0)	1	(2.5)	0	(0.0)	0	(0.0)	0	(0.0)	3	(1.7)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Event Summary by Race
Laboratory Adverse Events
Weeks 0-48

	Total											
	American Indian or Alaska Native		Asian		Black or African American		Multiple		Native Hawaiian or Other Pacific Islander		White	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	6		123		134		60		1		473	
with one or more adverse events	2	(33.3)	7	(5.7)	6	(4.5)	10	(16.7)	0	(0.0)	42	(8.9)
with no adverse event	4	(66.7)	116	(94.3)	128	(95.5)	50	(83.3)	1	(100.0)	431	(91.1)
with drug-related[†] adverse events	0	(0.0)	1	(0.8)	2	(1.5)	0	(0.0)	0	(0.0)	9	(1.9)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)	0	(0.0)	1	(0.2)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.7)	0	(0.0)	0	(0.0)	1	(0.2)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 53

Adverse Event Summary by Hepatitis B/C Status
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B and C Negative		Hepatitis B and/or C Positive		Hepatitis B and C Negative		Hepatitis B and/or C Positive		Hepatitis B and C Negative		Hepatitis B and/or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	516		15		258		8		774		23	
with one or more adverse events	426	(82.6)	13	(86.7)	224	(86.8)	7	(87.5)	650	(84.0)	20	(87.0)
with no adverse event	90	(17.4)	2	(13.3)	34	(13.2)	1	(12.5)	124	(16.0)	3	(13.0)
with drug-related[†] adverse events	129	(25.0)	1	(6.7)	64	(24.8)	4	(50.0)	193	(24.9)	5	(21.7)
with serious adverse events	31	(6.0)	0	(0.0)	22	(8.5)	3	(37.5)	53	(6.8)	3	(13.0)
with serious drug-related adverse events	1	(0.2)	0	(0.0)	1	(0.4)	1	(12.5)	2	(0.3)	1	(4.3)
who died	2	(0.4)	0	(0.0)	1	(0.4)	0	(0.0)	3	(0.4)	0	(0.0)
discontinued[‡] due to an adverse event	3	(0.6)	1	(6.7)	5	(1.9)	1	(12.5)	8	(1.0)	2	(8.7)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.8)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	3	(0.6)	0	(0.0)	1	(0.4)	1	(12.5)	4	(0.5)	1	(4.3)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 54

Subjects With Clinical Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	516		15		258		8		774		23	
with one or more adverse events	426	(82.6)	13	(86.7)	224	(86.8)	7	(87.5)	650	(84.0)	20	(87.0)
with no adverse events	90	(17.4)	2	(13.3)	34	(13.2)	1	(12.5)	124	(16.0)	3	(13.0)
Blood and lymphatic system disorders	**23**	**(4.5)**	**1**	**(6.7)**	**7**	**(2.7)**	**1**	**(12.5)**	**30**	**(3.9)**	**2**	**(8.7)**
Lymphadenopathy	14	(2.7)	1	(6.7)	4	(1.6)	1	(12.5)	18	(2.3)	2	(8.7)
Ear and labyrinth disorders	**13**	**(2.5)**	**1**	**(6.7)**	**8**	**(3.1)**	**0**	**(0.0)**	**21**	**(2.7)**	**1**	**(4.3)**
Ear pain	4	(0.8)	1	(6.7)	4	(1.6)	0	(0.0)	8	(1.0)	1	(4.3)
Eye disorders	**16**	**(3.1)**	**1**	**(6.7)**	**9**	**(3.5)**	**0**	**(0.0)**	**25**	**(3.2)**	**1**	**(4.3)**
Dry eye	1	(0.2)	1	(6.7)	0	(0.0)	0	(0.0)	1	(0.1)	1	(4.3)
Eye pruritus	2	(0.4)	1	(6.7)	1	(0.4)	0	(0.0)	3	(0.4)	1	(4.3)
Gastrointestinal disorders	**205**	**(39.7)**	**4**	**(26.7)**	**95**	**(36.8)**	**4**	**(50.0)**	**300**	**(38.8)**	**8**	**(34.8)**
Abdominal distension	10	(1.9)	0	(0.0)	7	(2.7)	1	(12.5)	17	(2.2)	1	(4.3)
Abdominal pain	39	(7.6)	1	(6.7)	10	(3.9)	1	(12.5)	49	(6.3)	2	(8.7)
Abdominal pain upper	12	(2.3)	1	(6.7)	4	(1.6)	0	(0.0)	16	(2.1)	1	(4.3)
Diarrhoea	56	(10.9)	2	(13.3)	29	(11.2)	1	(12.5)	85	(11.0)	3	(13.0)
Dyspepsia	12	(2.3)	0	(0.0)	5	(1.9)	2	(25.0)	17	(2.2)	2	(8.7)
Faeces hard	0	(0.0)	1	(6.7)	1	(0.4)	0	(0.0)	1	(0.1)	1	(4.3)
Gastrooesophageal reflux disease	8	(1.6)	0	(0.0)	7	(2.7)	1	(12.5)	15	(1.9)	1	(4.3)
Nausea	59	(11.4)	1	(6.7)	26	(10.1)	0	(0.0)	85	(11.0)	1	(4.3)
Vomiting	34	(6.6)	1	(6.7)	15	(5.8)	0	(0.0)	49	(6.3)	1	(4.3)

Subjects With Clinical Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**80**	**(15.5)**	**4**	**(26.7)**	**47**	**(18.2)**	**2**	**(25.0)**	**127**	**(16.4)**	**6**	**(26.1)**
Drug ineffective	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Fatigue	30	(5.8)	3	(20.0)	15	(5.8)	1	(12.5)	45	(5.8)	4	(17.4)
Pyrexia	20	(3.9)	1	(6.7)	11	(4.3)	0	(0.0)	31	(4.0)	1	(4.3)
Sluggishness	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Thirst	1	(0.2)	0	(0.0)	2	(0.8)	1	(12.5)	3	(0.4)	1	(4.3)
Immune system disorders	**8**	**(1.6)**	**1**	**(6.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**8**	**(1.0)**	**1**	**(4.3)**
Allergy to arthropod sting	0	(0.0)	1	(6.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.3)
Infections and infestations	**262**	**(50.8)**	**9**	**(60.0)**	**147**	**(57.0)**	**3**	**(37.5)**	**409**	**(52.8)**	**12**	**(52.2)**
Acute sinusitis	1	(0.2)	1	(6.7)	1	(0.4)	0	(0.0)	2	(0.3)	1	(4.3)
Cerebral toxoplasmosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Folliculitis	4	(0.8)	1	(6.7)	3	(1.2)	0	(0.0)	7	(0.9)	1	(4.3)
Hepatitis B	0	(0.0)	1	(6.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.3)
Latent tuberculosis	0	(0.0)	1	(6.7)	1	(0.4)	0	(0.0)	1	(0.1)	1	(4.3)
Nasopharyngitis	43	(8.3)	1	(6.7)	22	(8.5)	0	(0.0)	65	(8.4)	1	(4.3)
Penile abscess	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Pharyngitis	13	(2.5)	1	(6.7)	8	(3.1)	0	(0.0)	21	(2.7)	1	(4.3)
Rash pustular	0	(0.0)	1	(6.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.3)
Respiratory tract infection	5	(1.0)	1	(6.7)	2	(0.8)	0	(0.0)	7	(0.9)	1	(4.3)
Rhinitis	9	(1.7)	0	(0.0)	4	(1.6)	1	(12.5)	13	(1.7)	1	(4.3)
Syphilis	14	(2.7)	0	(0.0)	14	(5.4)	0	(0.0)	28	(3.6)	0	(0.0)
Tinea infection	1	(0.2)	1	(6.7)	0	(0.0)	0	(0.0)	1	(0.1)	1	(4.3)

Subjects With Clinical Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**262**	**(50.8)**	**9**	**(60.0)**	**147**	**(57.0)**	**3**	**(37.5)**	**409**	**(52.8)**	**12**	**(52.2)**
Tooth abscess	2	(0.4)	1	(6.7)	1	(0.4)	0	(0.0)	3	(0.4)	1	(4.3)
Tooth infection	6	(1.2)	1	(6.7)	0	(0.0)	0	(0.0)	6	(0.8)	1	(4.3)
Tuberculosis	1	(0.2)	1	(6.7)	1	(0.4)	1	(12.5)	2	(0.3)	2	(8.7)
Upper respiratory tract infection	40	(7.8)	0	(0.0)	19	(7.4)	0	(0.0)	59	(7.6)	0	(0.0)
Urethritis gonococcal	1	(0.2)	1	(6.7)	2	(0.8)	0	(0.0)	3	(0.4)	1	(4.3)
Urinary tract infection	10	(1.9)	1	(6.7)	3	(1.2)	0	(0.0)	13	(1.7)	1	(4.3)
Injury, poisoning and procedural complications	**57**	**(11.0)**	**0**	**(0.0)**	**27**	**(10.5)**	**1**	**(12.5)**	**84**	**(10.9)**	**1**	**(4.3)**
Contusion	2	(0.4)	0	(0.0)	0	(0.0)	1	(12.5)	2	(0.3)	1	(4.3)
Metabolism and nutrition disorders	**26**	**(5.0)**	**1**	**(6.7)**	**11**	**(4.3)**	**2**	**(25.0)**	**37**	**(4.8)**	**3**	**(13.0)**
Decreased appetite	13	(2.5)	1	(6.7)	0	(0.0)	0	(0.0)	13	(1.7)	1	(4.3)
Increased appetite	3	(0.6)	0	(0.0)	0	(0.0)	1	(12.5)	3	(0.4)	1	(4.3)
Vitamin D deficiency	4	(0.8)	0	(0.0)	4	(1.6)	1	(12.5)	8	(1.0)	1	(4.3)
Musculoskeletal and connective tissue disorders	**86**	**(16.7)**	**3**	**(20.0)**	**34**	**(13.2)**	**2**	**(25.0)**	**120**	**(15.5)**	**5**	**(21.7)**
Arthralgia	15	(2.9)	1	(6.7)	6	(2.3)	0	(0.0)	21	(2.7)	1	(4.3)
Back pain	23	(4.5)	1	(6.7)	8	(3.1)	0	(0.0)	31	(4.0)	1	(4.3)
Monarthritis	0	(0.0)	1	(6.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.3)
Neck pain	7	(1.4)	0	(0.0)	1	(0.4)	1	(12.5)	8	(1.0)	1	(4.3)
Tendonitis	2	(0.4)	0	(0.0)	2	(0.8)	1	(12.5)	4	(0.5)	1	(4.3)
Nervous system disorders	**120**	**(23.3)**	**2**	**(13.3)**	**53**	**(20.5)**	**1**	**(12.5)**	**173**	**(22.4)**	**3**	**(13.0)**
Headache	69	(13.4)	2	(13.3)	28	(10.9)	1	(12.5)	97	(12.5)	3	(13.0)

Subjects With Clinical Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**120**	**(23.3)**	**2**	**(13.3)**	**53**	**(20.5)**	**1**	**(12.5)**	**173**	**(22.4)**	**3**	**(13.0)**
Syncope	4	(0.8)	0	(0.0)	2	(0.8)	1	(12.5)	6	(0.8)	1	(4.3)
Psychiatric disorders	**70**	**(13.6)**	**1**	**(6.7)**	**42**	**(16.3)**	**1**	**(12.5)**	**112**	**(14.5)**	**2**	**(8.7)**
Abnormal dreams	14	(2.7)	1	(6.7)	7	(2.7)	0	(0.0)	21	(2.7)	1	(4.3)
Insomnia	21	(4.1)	0	(0.0)	13	(5.0)	0	(0.0)	34	(4.4)	0	(0.0)
Nervousness	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Renal and urinary disorders	**13**	**(2.5)**	**0**	**(0.0)**	**5**	**(1.9)**	**1**	**(12.5)**	**18**	**(2.3)**	**1**	**(4.3)**
Renal failure	2	(0.4)	0	(0.0)	1	(0.4)	1	(12.5)	3	(0.4)	1	(4.3)
Reproductive system and breast disorders	**35**	**(6.8)**	**0**	**(0.0)**	**9**	**(3.5)**	**0**	**(0.0)**	**44**	**(5.7)**	**0**	**(0.0)**
Respiratory, thoracic and mediastinal disorders	**75**	**(14.5)**	**1**	**(6.7)**	**40**	**(15.5)**	**0**	**(0.0)**	**115**	**(14.9)**	**1**	**(4.3)**
Cough	27	(5.2)	1	(6.7)	14	(5.4)	0	(0.0)	41	(5.3)	1	(4.3)
Rhinitis allergic	14	(2.7)	1	(6.7)	6	(2.3)	0	(0.0)	20	(2.6)	1	(4.3)
Skin and subcutaneous tissue disorders	**100**	**(19.4)**	**1**	**(6.7)**	**62**	**(24.0)**	**1**	**(12.5)**	**162**	**(20.9)**	**2**	**(8.7)**
Pruritus	14	(2.7)	1	(6.7)	15	(5.8)	0	(0.0)	29	(3.7)	1	(4.3)
Rash	22	(4.3)	1	(6.7)	11	(4.3)	0	(0.0)	33	(4.3)	1	(4.3)
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(4.3)
Vascular disorders	**25**	**(4.8)**	**0**	**(0.0)**	**9**	**(3.5)**	**2**	**(25.0)**	**34**	**(4.4)**	**2**	**(8.7)**
Hot flush	3	(0.6)	0	(0.0)	0	(0.0)	1	(12.5)	3	(0.4)	1	(4.3)

Subjects With Clinical Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	**25**	**(4.8)**	**0**	**(0.0)**	**9**	**(3.5)**	**2**	**(25.0)**	**34**	**(4.4)**	**2**	**(8.7)**
Hypertension	16	(3.1)	0	(0.0)	6	(2.3)	1	(12.5)	22	(2.8)	1	(4.3)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 55

Adverse Event Summary by Hepatitis B/C Status
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B and C Negative		Hepatitis B and/or C Positive		Hepatitis B and C Negative		Hepatitis B and/or C Positive		Hepatitis B and C Negative		Hepatitis B and/or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	516		15		258		8		774		23	
with one or more adverse events	35	(6.8)	2	(13.3)	30	(11.6)	0	(0.0)	65	(8.4)	2	(8.7)
with no adverse event	481	(93.2)	13	(86.7)	228	(88.4)	8	(100.0)	709	(91.6)	21	(91.3)
with drug-related[†] adverse events	7	(1.4)	1	(6.7)	4	(1.6)	0	(0.0)	11	(1.4)	1	(4.3)
with serious adverse events	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a drug-related adverse event	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 56

Subjects With Laboratory Adverse Events by Hepatitis B/C Status (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive		Hepatitis B And C Negative		Hepatitis B And/Or C Positive	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	516		15		258		8		774		23	
with one or more adverse events	35	(6.8)	2	(13.3)	30	(11.6)	0	(0.0)	65	(8.4)	2	(8.7)
with no adverse events	481	(93.2)	13	(86.7)	228	(88.4)	8	(100.0)	709	(91.6)	21	(91.3)
Investigations	**35**	**(6.8)**	**2**	**(13.3)**	**30**	**(11.6)**	**0**	**(0.0)**	**65**	**(8.4)**	**2**	**(8.7)**
Alanine aminotransferase increased	7	(1.4)	2	(13.3)	3	(1.2)	0	(0.0)	10	(1.3)	2	(8.7)
Aspartate aminotransferase increased	12	(2.3)	2	(13.3)	5	(1.9)	0	(0.0)	17	(2.2)	2	(8.7)
Blood creatine phosphokinase increased	18	(3.5)	0	(0.0)	17	(6.6)	0	(0.0)	35	(4.5)	0	(0.0)
Eosinophil count increased	2	(0.4)	1	(6.7)	1	(0.4)	0	(0.0)	3	(0.4)	1	(4.3)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 57

Subjects With Laboratory Findings That Met Predetermined Criteria
Hepatitis B and C Negative; Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
HEMATOLOGY						
Neutrophils (10[3]/microL)						
Grade 1:1.00 - 1.30	20/515	(3.9)	10/257	(3.9)	30/772	(3.9)
Grade 2:0.75 - 0.999	6/515	(1.2)	1/257	(0.4)	7/772	(0.9)
Grade 3:0.50 - 0.749	5/515	(1.0)	3/257	(1.2)	8/772	(1.0)
Grade 4:<0.50	0/515	(0.0)	0/257	(0.0)	0/772	(0.0)
Hemoglobin (gm/dL)						
Grade 1:8.5 - 10.0	5/515	(1.0)	1/258	(0.4)	6/773	(0.8)
Grade 2:7.5 - 8.4	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Grade 3:6.5 - 7.4	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Grade 4:< 6.5	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Platelets (10[3]/microL)						
Grade 1:100 - 124.999	6/515	(1.2)	4/258	(1.6)	10/773	(1.3)
Grade 2:50 - 99.999	4/515	(0.8)	1/258	(0.4)	5/773	(0.6)
Grade 3:25 - 49.999	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Grade 4:<25	0/515	(0.0)	1/258	(0.4)	1/773	(0.1)
CHEMISTRY						
Total Bilirubin (mg/dL)						
Grade 1:1.1 - 1.5 x ULN	27/515	(5.2)	14/258	(5.4)	41/773	(5.3)
Grade 2:1.6 - 2.5 x ULN	6/515	(1.2)	2/258	(0.8)	8/773	(1.0)
Grade 3:2.6 - 5.0 x ULN	3/515	(0.6)	0/258	(0.0)	3/773	(0.4)
Grade 4:>5.0 x ULN	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Creatinine (mg/dL)						
Grade 1:1.1 - 1.3 x ULN	3/515	(0.6)	2/258	(0.8)	5/773	(0.6)
Grade 2:1.4 - 1.8 x ULN	0/515	(0.0)	1/258	(0.4)	1/773	(0.1)
Grade 3:1.9 - 3.4 x ULN	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Grade 4:≥3.5 x ULN	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Aspartate Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	36/515	(7.0)	28/258	(10.9)	64/773	(8.3)
Grade 2:2.6 - 5.0 x ULN	15/515	(2.9)	5/258	(1.9)	20/773	(2.6)
Grade 3:5.1 - 10.0 x ULN	6/515	(1.2)	1/258	(0.4)	7/773	(0.9)
Grade 4:>10.0 x ULN	1/515	(0.2)	0/258	(0.0)	1/773	(0.1)
Alanine Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	48/515	(9.3)	33/258	(12.8)	81/773	(10.5)
Grade 2:2.6 - 5.0 x ULN	9/515	(1.7)	1/258	(0.4)	10/773	(1.3)
Grade 3:5.1 - 10.0 x ULN	5/515	(1.0)	1/258	(0.4)	6/773	(0.8)
Grade 4:>10.0 x ULN	1/515	(0.2)	0/258	(0.0)	1/773	(0.1)

Subjects With Laboratory Findings That Met Predetermined Criteria
Hepatitis B and C Negative; Worsening Grade; Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
Alkaline Phosphatase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	11/515	(2.1)	3/258	(1.2)	14/773	(1.8)
Grade 2:2.6 - 5.0 x ULN	6/515	(1.2)	0/258	(0.0)	6/773	(0.8)
Grade 3:5.1 - 10.0 x ULN	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Grade 4:>10.0 x ULN	0/515	(0.0)	0/258	(0.0)	0/773	(0.0)
Lipase (IU/L)						
Grade 1:1.1 - 1.5 x ULN	33/515	(6.4)	23/258	(8.9)	56/773	(7.2)
Grade 2:1.6 - 3.0 x ULN	25/515	(4.9)	11/258	(4.3)	36/773	(4.7)
Grade 3:3.1 - 5.0 x ULN	7/515	(1.4)	1/258	(0.4)	8/773	(1.0)
Grade 4:>5.0 x ULN	5/515	(1.0)	0/258	(0.0)	5/773	(0.6)
Creatine Kinase (IU/L)						
Grade 1:3.0 - 5.9 x ULN	31/515	(6.0)	20/258	(7.8)	51/773	(6.6)
Grade 2:6.0 - 9.9 x ULN	16/515	(3.1)	6/258	(2.3)	22/773	(2.8)
Grade 3:10.0 - 19.9 x ULN	6/515	(1.2)	7/258	(2.7)	13/773	(1.7)
Grade 4:≥ 20.0 x ULN	10/515	(1.9)	4/258	(1.6)	14/773	(1.8)

[†]For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A subject was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 58

Subjects With Laboratory Findings That Met Predetermined Criteria
Hepatitis B and/or C Positive; Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
HEMATOLOGY						
Neutrophils (10[3]/microL)						
Grade 1:1.00 - 1.30	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 2:0.75 - 0.999	1/15	(6.7)	1/8	(12.5)	2/23	(8.7)
Grade 3:0.50 - 0.749	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:<0.50	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Hemoglobin (gm/dL)						
Grade 1:8.5 - 10.0	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 2:7.5 - 8.4	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 3:6.5 - 7.4	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:< 6.5	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Platelets (10[3]/microL)						
Grade 1:100 - 124.999	1/14	(7.1)	1/8	(12.5)	2/22	(9.1)
Grade 2:50 - 99.999	0/14	(0.0)	0/8	(0.0)	0/22	(0.0)
Grade 3:25 - 49.999	0/14	(0.0)	0/8	(0.0)	0/22	(0.0)
Grade 4:<25	0/14	(0.0)	0/8	(0.0)	0/22	(0.0)
CHEMISTRY						
Total Bilirubin (mg/dL)						
Grade 1:1.1 - 1.5 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 2:1.6 - 2.5 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 3:2.6 - 5.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:>5.0 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Creatinine (mg/dL)						
Grade 1:1.1 - 1.3 x ULN	1/15	(6.7)	1/8	(12.5)	2/23	(8.7)
Grade 2:1.4 - 1.8 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 3:1.9 - 3.4 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:≥3.5 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Aspartate Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	3/15	(20.0)	1/8	(12.5)	4/23	(17.4)
Grade 2:2.6 - 5.0 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 3:5.1 - 10.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:>10.0 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Alanine Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 2:2.6 - 5.0 x ULN	4/15	(26.7)	1/8	(12.5)	5/23	(21.7)
Grade 3:5.1 - 10.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:>10.0 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)

Subjects With Laboratory Findings That Met Predetermined Criteria
Hepatitis B and/or C Positive; Worsening Grade; Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
Alkaline Phosphatase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 2:2.6 - 5.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 3:5.1 - 10.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:>10.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Lipase (IU/L)						
Grade 1:1.1 - 1.5 x ULN	2/15	(13.3)	2/8	(25.0)	4/23	(17.4)
Grade 2:1.6 - 3.0 x ULN	2/15	(13.3)	1/8	(12.5)	3/23	(13.0)
Grade 3:3.1 - 5.0 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 4:>5.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Creatine Kinase (IU/L)						
Grade 1:3.0 - 5.9 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 2:6.0 - 9.9 x ULN	1/15	(6.7)	0/8	(0.0)	1/23	(4.3)
Grade 3:10.0 - 19.9 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)
Grade 4:≥ 20.0 x ULN	0/15	(0.0)	0/8	(0.0)	0/23	(0.0)

[†]For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A subject was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 59

Adverse Event Summary by Concomitant Use of Proton Pump Inhibitors/H2 Blockers
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker		with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker		with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	61		470		42		224		103		694	
with one or more adverse events	59	(96.7)	380	(80.9)	39	(92.9)	192	(85.7)	98	(95.1)	572	(82.4)
with no adverse event	2	(3.3)	90	(19.1)	3	(7.1)	32	(14.3)	5	(4.9)	122	(17.6)
with drug-related[†] adverse events	14	(23.0)	116	(24.7)	12	(28.6)	56	(25.0)	26	(25.2)	172	(24.8)
with serious adverse events	5	(8.2)	26	(5.5)	10	(23.8)	15	(6.7)	15	(14.6)	41	(5.9)
with serious drug-related adverse events	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.9)	0	(0.0)	3	(0.4)
who died	0	(0.0)	2	(0.4)	1	(2.4)	0	(0.0)	1	(1.0)	2	(0.3)
discontinued[‡] due to an adverse event	0	(0.0)	4	(0.9)	1	(2.4)	5	(2.2)	1	(1.0)	9	(1.3)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.9)	0	(0.0)	2	(0.3)
discontinued due to a serious adverse event	0	(0.0)	3	(0.6)	1	(2.4)	1	(0.4)	1	(1.0)	4	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 60

Subjects With Clinical Adverse Events by Concomitant Use of Proton Pump Inhibitors/H2 Blockers (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	61		470		42		224		103		694	
with one or more adverse events	59	(96.7)	380	(80.9)	39	(92.9)	192	(85.7)	98	(95.1)	572	(82.4)
with no adverse events	2	(3.3)	90	(19.1)	3	(7.1)	32	(14.3)	5	(4.9)	122	(17.6)
Blood and lymphatic system disorders	**3**	**(4.9)**	**21**	**(4.5)**	**3**	**(7.1)**	**5**	**(2.2)**	**6**	**(5.8)**	**26**	**(3.7)**
Ear and labyrinth disorders	**5**	**(8.2)**	**9**	**(1.9)**	**0**	**(0.0)**	**8**	**(3.6)**	**5**	**(4.9)**	**17**	**(2.4)**
Gastrointestinal disorders	**46**	**(75.4)**	**163**	**(34.7)**	**30**	**(71.4)**	**69**	**(30.8)**	**76**	**(73.8)**	**232**	**(33.4)**
Abdominal distension	3	(4.9)	7	(1.5)	3	(7.1)	5	(2.2)	6	(5.8)	12	(1.7)
Abdominal pain	10	(16.4)	30	(6.4)	5	(11.9)	6	(2.7)	15	(14.6)	36	(5.2)
Abdominal pain upper	6	(9.8)	7	(1.5)	2	(4.8)	2	(0.9)	8	(7.8)	9	(1.3)
Constipation	7	(11.5)	7	(1.5)	0	(0.0)	4	(1.8)	7	(6.8)	11	(1.6)
Diarrhoea	8	(13.1)	50	(10.6)	9	(21.4)	21	(9.4)	17	(16.5)	71	(10.2)
Dyspepsia	5	(8.2)	7	(1.5)	4	(9.5)	3	(1.3)	9	(8.7)	10	(1.4)
Gastritis	3	(4.9)	0	(0.0)	6	(14.3)	0	(0.0)	9	(8.7)	0	(0.0)
Gastrooesophageal reflux disease	6	(9.8)	2	(0.4)	7	(16.7)	1	(0.4)	13	(12.6)	3	(0.4)
Haemorrhoids	4	(6.6)	2	(0.4)	1	(2.4)	2	(0.9)	5	(4.9)	4	(0.6)
Nausea	14	(23.0)	46	(9.8)	7	(16.7)	19	(8.5)	21	(20.4)	65	(9.4)
Vomiting	9	(14.8)	26	(5.5)	3	(7.1)	12	(5.4)	12	(11.7)	38	(5.5)
General disorders and administration site conditions	**14**	**(23.0)**	**70**	**(14.9)**	**14**	**(33.3)**	**35**	**(15.6)**	**28**	**(27.2)**	**105**	**(15.1)**

Subjects With Clinical Adverse Events by Concomitant Use of Proton Pump Inhibitors/H2 Blockers (Incidence ≥ 5% in Any Column) Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**14**	**(23.0)**	**70**	**(14.9)**	**14**	**(33.3)**	**35**	**(15.6)**	**28**	**(27.2)**	**105**	**(15.1)**
Fatigue	6	(9.8)	27	(5.7)	4	(9.5)	12	(5.4)	10	(9.7)	39	(5.6)
Influenza like illness	2	(3.3)	7	(1.5)	3	(7.1)	8	(3.6)	5	(4.9)	15	(2.2)
Pyrexia	3	(4.9)	18	(3.8)	5	(11.9)	6	(2.7)	8	(7.8)	24	(3.5)
Infections and infestations	**42**	**(68.9)**	**229**	**(48.7)**	**29**	**(69.0)**	**121**	**(54.0)**	**71**	**(68.9)**	**350**	**(50.4)**
Gastroenteritis	6	(9.8)	10	(2.1)	2	(4.8)	9	(4.0)	8	(7.8)	19	(2.7)
Influenza	6	(9.8)	12	(2.6)	3	(7.1)	9	(4.0)	9	(8.7)	21	(3.0)
Nasopharyngitis	6	(9.8)	38	(8.1)	6	(14.3)	16	(7.1)	12	(11.7)	54	(7.8)
Syphilis	2	(3.3)	12	(2.6)	1	(2.4)	13	(5.8)	3	(2.9)	25	(3.6)
Upper respiratory tract infection	6	(9.8)	34	(7.2)	4	(9.5)	15	(6.7)	10	(9.7)	49	(7.1)
Injury, poisoning and procedural complications	**11**	**(18.0)**	**46**	**(9.8)**	**8**	**(19.0)**	**20**	**(8.9)**	**19**	**(18.4)**	**66**	**(9.5)**
Accidental overdose	4	(6.6)	18	(3.8)	1	(2.4)	9	(4.0)	5	(4.9)	27	(3.9)
Metabolism and nutrition disorders	**6**	**(9.8)**	**21**	**(4.5)**	**5**	**(11.9)**	**8**	**(3.6)**	**11**	**(10.7)**	**29**	**(4.2)**
Decreased appetite	5	(8.2)	9	(1.9)	0	(0.0)	0	(0.0)	5	(4.9)	9	(1.3)
Musculoskeletal and connective tissue disorders	**23**	**(37.7)**	**66**	**(14.0)**	**12**	**(28.6)**	**24**	**(10.7)**	**35**	**(34.0)**	**90**	**(13.0)**
Back pain	5	(8.2)	19	(4.0)	5	(11.9)	3	(1.3)	10	(9.7)	22	(3.2)
Myalgia	5	(8.2)	14	(3.0)	3	(7.1)	4	(1.8)	8	(7.8)	18	(2.6)

Subjects With Clinical Adverse Events by Concomitant Use of Proton Pump Inhibitors/H2 Blockers (Incidence ≥ 5% in Any Column) Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**(6.6)**	**21**	**(4.5)**	**4**	**(9.5)**	**6**	**(2.7)**	**8**	**(7.8)**	**27**	**(3.9)**
Nervous system disorders	**19**	**(31.1)**	**103**	**(21.9)**	**10**	**(23.8)**	**44**	**(19.6)**	**29**	**(28.2)**	**147**	**(21.2)**
Dizziness	2	(3.3)	22	(4.7)	0	(0.0)	12	(5.4)	2	(1.9)	34	(4.9)
Headache	11	(18.0)	60	(12.8)	8	(19.0)	21	(9.4)	19	(18.4)	81	(11.7)
Psychiatric disorders	**7**	**(11.5)**	**64**	**(13.6)**	**8**	**(19.0)**	**35**	**(15.6)**	**15**	**(14.6)**	**99**	**(14.3)**
Insomnia	5	(8.2)	16	(3.4)	1	(2.4)	12	(5.4)	6	(5.8)	28	(4.0)
Renal and urinary disorders	**4**	**(6.6)**	**9**	**(1.9)**	**1**	**(2.4)**	**5**	**(2.2)**	**5**	**(4.9)**	**14**	**(2.0)**
Reproductive system and breast disorders	**7**	**(11.5)**	**28**	**(6.0)**	**2**	**(4.8)**	**7**	**(3.1)**	**9**	**(8.7)**	**35**	**(5.0)**
Respiratory, thoracic and mediastinal disorders	**14**	**(23.0)**	**62**	**(13.2)**	**6**	**(14.3)**	**34**	**(15.2)**	**20**	**(19.4)**	**96**	**(13.8)**
Cough	4	(6.6)	24	(5.1)	2	(4.8)	12	(5.4)	6	(5.8)	36	(5.2)
Oropharyngeal pain	5	(8.2)	15	(3.2)	2	(4.8)	7	(3.1)	7	(6.8)	22	(3.2)
Skin and subcutaneous tissue disorders	**15**	**(24.6)**	**86**	**(18.3)**	**13**	**(31.0)**	**50**	**(22.3)**	**28**	**(27.2)**	**136**	**(19.6)**
Pruritus	3	(4.9)	12	(2.6)	1	(2.4)	14	(6.3)	4	(3.9)	26	(3.7)
Rash	2	(3.3)	21	(4.5)	5	(11.9)	6	(2.7)	7	(6.8)	27	(3.9)

Subjects With Clinical Adverse Events by Concomitant Use of Proton Pump Inhibitors/H2 Blockers (Incidence ≥ 5% in Any Column) Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	**5**	**(8.2)**	**20**	**(4.3)**	**3**	**(7.1)**	**8**	**(3.6)**	**8**	**(7.8)**	**28**	**(4.0)**

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 61

Adverse Event Summary by Concomitant Use of Proton Pump Inhibitors/H2 Blockers
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker		with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker		with concomitant use of PPI/H2 blocker		without concomitant use of PPI/H2 blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	61		470		42		224		103		694	
with one or more adverse events	5	(8.2)	32	(6.8)	8	(19.0)	22	(9.8)	13	(12.6)	54	(7.8)
with no adverse event	56	(91.8)	438	(93.2)	34	(81.0)	202	(90.2)	90	(87.4)	640	(92.2)
with drug-related[†] adverse events	1	(1.6)	7	(1.5)	1	(2.4)	3	(1.3)	2	(1.9)	10	(1.4)
with serious adverse events	0	(0.0)	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
discontinued due to a drug-related adverse event	0	(0.0)	2	(0.4)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 62

Subjects With Laboratory Adverse Events by Concomitant Use of Proton Pump Inhibitors/H2 Blockers (Incidence ≥ 5% in Any Column)
Weeks 0-48

	Raltegravir 1200 mg QD				Raltegravir 400 mg BID				Total			
	With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker		With Concomitant Use Of Ppi/H2 Blocker		Without Concomitant Use Of Ppi/H2 Blocker	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	61		470		42		224		103		694	
with one or more adverse events	5	(8.2)	32	(6.8)	8	(19.0)	22	(9.8)	13	(12.6)	54	(7.8)
with no adverse events	56	(91.8)	438	(93.2)	34	(81.0)	202	(90.2)	90	(87.4)	640	(92.2)
Investigations	**5**	**(8.2)**	**32**	**(6.8)**	**8**	**(19.0)**	**22**	**(9.8)**	**13**	**(12.6)**	**54**	**(7.8)**
Blood creatine phosphokinase increased	3	(4.9)	15	(3.2)	4	(9.5)	13	(5.8)	7	(6.8)	28	(4.0)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 63

Subjects With Laboratory Findings That Met Predetermined Criteria
Concomitant Use of Proton Pump Inhibitors/H2 Blockers; Worsening Grade; Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
HEMATOLOGY						
Neutrophils (10[3]/microL)						
Grade 1:1.00 - 1.30	2/61	(3.3)	1/42	(2.4)	3/103	(2.9)
Grade 2:0.75 - 0.999	0/61	(0.0)	1/42	(2.4)	1/103	(1.0)
Grade 3:0.50 - 0.749	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:<0.50	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Hemoglobin (gm/dL)						
Grade 1:8.5 - 10.0	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 2:7.5 - 8.4	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 3:6.5 - 7.4	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:< 6.5	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Platelets (10[3]/microL)						
Grade 1:100 - 124.999	0/61	(0.0)	2/42	(4.8)	2/103	(1.9)
Grade 2:50 - 99.999	0/61	(0.0)	1/42	(2.4)	1/103	(1.0)
Grade 3:25 - 49.999	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:<25	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
CHEMISTRY						
Total Bilirubin (mg/dL)						
Grade 1:1.1 - 1.5 x ULN	4/61	(6.6)	1/42	(2.4)	5/103	(4.9)
Grade 2:1.6 - 2.5 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 3:2.6 - 5.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:>5.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Creatinine (mg/dL)						
Grade 1:1.1 - 1.3 x ULN	0/61	(0.0)	2/42	(4.8)	2/103	(1.9)
Grade 2:1.4 - 1.8 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 3:1.9 - 3.4 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:≥3.5 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Aspartate Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	4/61	(6.6)	6/42	(14.3)	10/103	(9.7)
Grade 2:2.6 - 5.0 x ULN	1/61	(1.6)	1/42	(2.4)	2/103	(1.9)
Grade 3:5.1 - 10.0 x ULN	4/61	(6.6)	0/42	(0.0)	4/103	(3.9)
Grade 4:>10.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Alanine Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	7/61	(11.5)	7/42	(16.7)	14/103	(13.6)
Grade 2:2.6 - 5.0 x ULN	1/61	(1.6)	0/42	(0.0)	1/103	(1.0)
Grade 3:5.1 - 10.0 x ULN	3/61	(4.9)	0/42	(0.0)	3/103	(2.9)
Grade 4:>10.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)

Subjects With Laboratory Findings That Met Predetermined Criteria
Concomitant Use of Proton Pump Inhibitors/H2 Blockers; Worsening Grade; Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
Alkaline Phosphatase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	4/61	(6.6)	0/42	(0.0)	4/103	(3.9)
Grade 2:2.6 - 5.0 x ULN	1/61	(1.6)	0/42	(0.0)	1/103	(1.0)
Grade 3:5.1 - 10.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:>10.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Lipase (IU/L)						
Grade 1:1.1 - 1.5 x ULN	5/61	(8.2)	4/42	(9.5)	9/103	(8.7)
Grade 2:1.6 - 3.0 x ULN	3/61	(4.9)	4/42	(9.5)	7/103	(6.8)
Grade 3:3.1 - 5.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Grade 4:>5.0 x ULN	0/61	(0.0)	0/42	(0.0)	0/103	(0.0)
Creatine Kinase (IU/L)						
Grade 1:3.0 - 5.9 x ULN	3/61	(4.9)	1/42	(2.4)	4/103	(3.9)
Grade 2:6.0 - 9.9 x ULN	2/61	(3.3)	0/42	(0.0)	2/103	(1.9)
Grade 3:10.0 - 19.9 x ULN	1/61	(1.6)	2/42	(4.8)	3/103	(2.9)
Grade 4:≥ 20.0 x ULN	2/61	(3.3)	0/42	(0.0)	2/103	(1.9)

[†]For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A subject was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 64

Subjects With Laboratory Findings That Met Predetermined Criteria Without Concomitant Use of Proton Pump Inhibitors/H2 Blockers; Worsening Grade Weeks 0-48

Criterion†	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
HEMATOLOGY						
Neutrophils (10[3]/microL)						
Grade 1:1.00 - 1.30	19/469	(4.1)	9/223	(4.0)	28/692	(4.0)
Grade 2:0.75 - 0.999	7/469	(1.5)	1/223	(0.4)	8/692	(1.2)
Grade 3:0.50 - 0.749	5/469	(1.1)	3/223	(1.3)	8/692	(1.2)
Grade 4:<0.50	0/469	(0.0)	0/223	(0.0)	0/692	(0.0)
Hemoglobin (gm/dL)						
Grade 1:8.5 - 10.0	5/469	(1.1)	1/224	(0.4)	6/693	(0.9)
Grade 2:7.5 - 8.4	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Grade 3:6.5 - 7.4	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Grade 4:< 6.5	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Platelets (10[3]/microL)						
Grade 1:100 - 124.999	7/468	(1.5)	3/224	(1.3)	10/692	(1.4)
Grade 2:50 - 99.999	4/468	(0.9)	0/224	(0.0)	4/692	(0.6)
Grade 3:25 - 49.999	0/468	(0.0)	0/224	(0.0)	0/692	(0.0)
Grade 4:<25	0/468	(0.0)	1/224	(0.4)	1/692	(0.1)
CHEMISTRY						
Total Bilirubin (mg/dL)						
Grade 1:1.1 - 1.5 x ULN	23/469	(4.9)	13/224	(5.8)	36/693	(5.2)
Grade 2:1.6 - 2.5 x ULN	7/469	(1.5)	2/224	(0.9)	9/693	(1.3)
Grade 3:2.6 - 5.0 x ULN	3/469	(0.6)	0/224	(0.0)	3/693	(0.4)
Grade 4:>5.0 x ULN	1/469	(0.2)	0/224	(0.0)	1/693	(0.1)
Creatinine (mg/dL)						
Grade 1:1.1 - 1.3 x ULN	4/469	(0.9)	1/224	(0.4)	5/693	(0.7)
Grade 2:1.4 - 1.8 x ULN	0/469	(0.0)	1/224	(0.4)	1/693	(0.1)
Grade 3:1.9 - 3.4 x ULN	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Grade 4:≥3.5 x ULN	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Aspartate Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	35/469	(7.5)	23/224	(10.3)	58/693	(8.4)
Grade 2:2.6 - 5.0 x ULN	15/469	(3.2)	4/224	(1.8)	19/693	(2.7)
Grade 3:5.1 - 10.0 x ULN	2/469	(0.4)	1/224	(0.4)	3/693	(0.4)
Grade 4:>10.0 x ULN	2/469	(0.4)	0/224	(0.0)	2/693	(0.3)
Alanine Aminotransferase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	42/469	(9.0)	26/224	(11.6)	68/693	(9.8)
Grade 2:2.6 - 5.0 x ULN	12/469	(2.6)	2/224	(0.9)	14/693	(2.0)
Grade 3:5.1 - 10.0 x ULN	2/469	(0.4)	1/224	(0.4)	3/693	(0.4)
Grade 4:>10.0 x ULN	2/469	(0.4)	0/224	(0.0)	2/693	(0.3)

Subjects With Laboratory Findings That Met Predetermined Criteria Without Concomitant Use of Proton Pump Inhibitors/H2 Blockers; Worsening Grade Weeks 0-48

Criterion[†]	Raltegravir 1200 mg QD		Raltegravir 400 mg BID		Total	
	n/m	(%)	n/m	(%)	n/m	(%)
Alkaline Phosphatase (IU/L)						
Grade 1:1.25 - 2.5 x ULN	8/469	(1.7)	3/224	(1.3)	11/693	(1.6)
Grade 2:2.6 - 5.0 x ULN	5/469	(1.1)	0/224	(0.0)	5/693	(0.7)
Grade 3:5.1 - 10.0 x ULN	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Grade 4:>10.0 x ULN	0/469	(0.0)	0/224	(0.0)	0/693	(0.0)
Lipase (IU/L)						
Grade 1:1.1 - 1.5 x ULN	30/469	(6.4)	21/224	(9.4)	51/693	(7.4)
Grade 2:1.6 - 3.0 x ULN	24/469	(5.1)	8/224	(3.6)	32/693	(4.6)
Grade 3:3.1 - 5.0 x ULN	8/469	(1.7)	1/224	(0.4)	9/693	(1.3)
Grade 4:>5.0 x ULN	5/469	(1.1)	0/224	(0.0)	5/693	(0.7)
Creatine Kinase (IU/L)						
Grade 1:3.0 - 5.9 x ULN	28/469	(6.0)	19/224	(8.5)	47/693	(6.8)
Grade 2:6.0 - 9.9 x ULN	15/469	(3.2)	6/224	(2.7)	21/693	(3.0)
Grade 3:10.0 - 19.9 x ULN	5/469	(1.1)	5/224	(2.2)	10/693	(1.4)
Grade 4:≥ 20.0 x ULN	8/469	(1.7)	4/224	(1.8)	12/693	(1.7)

[†]For graded criteria: subjects are counted once per test in the highest grade reported.

For inclusion in this analysis, both a baseline and at least one on-treatment laboratory value had to be present. Only subjects with a worsened grade from baseline were included. A subject was listed with a Grade X event if his/her highest grade during treatment was X.

n = Number of subjects with postbaseline test results that met the predetermined criterion.

m = Number of subjects with at least one postbaseline test result.

LLN = Lower limit of normal range. ULN = Upper limit of normal range.

Note: Raltegravir 1200 mg QD and Raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 65

Adverse Event Summary by Raltegravir Cmax Quartile
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD							
	Cmax 1st Quartile		Cmax 2nd Quartile		Cmax 3rd Quartile		Cmax 4th Quartile	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	134		128		132		130	
with one or more adverse events	103	(76.9)	106	(82.8)	111	(84.1)	112	(86.2)
with no adverse event	31	(23.1)	22	(17.2)	21	(15.9)	18	(13.8)
with drug-related[†] adverse events	30	(22.4)	34	(26.6)	34	(25.8)	28	(21.5)
with serious adverse events	6	(4.5)	5	(3.9)	4	(3.0)	14	(10.8)
with serious drug-related adverse events	0	(0.0)	1	(0.8)	0	(0.0)	0	(0.0)
who died	1	(0.7)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	1	(0.7)	0	(0.0)	1	(0.8)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	1	(0.7)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Cmax quartiles: Q1= 13100 (nM), median= 16850 (nM), Q3= 20500 (nM).
Cmax= Cmax (nM) at steady state.
Note: Raltegravir 1200 mg QD were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 66

Adverse Event Summary by Raltegravir AUC Quartile
Clinical Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD							
	AUC 1st Quartile		AUC 2nd Quartile		AUC 3rd Quartile		AUC 4th Quartile	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	131		133		130		130	
with one or more adverse events	104	(79.4)	109	(82.0)	109	(83.8)	110	(84.6)
with no adverse event	27	(20.6)	24	(18.0)	21	(16.2)	20	(15.4)
with drug-related[†] adverse events	27	(20.6)	37	(27.8)	34	(26.2)	28	(21.5)
with serious adverse events	6	(4.6)	4	(3.0)	8	(6.2)	11	(8.5)
with serious drug-related adverse events	0	(0.0)	1	(0.8)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	1	(0.8)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	2	(1.5)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(0.8)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
AUC quartiles: Q1= 42250 (nM*h), median= 54600 (nM*h), Q3= 69000 (nM*h).
AUC= AUC0-24h (nM*h) at steady state.
Note: Raltegravir 1200 mg QD were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 67

Adverse Event Summary by Raltegravir Cmax Quartile
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD							
	Cmax 1st Quartile		Cmax 2nd Quartile		Cmax 3rd Quartile		Cmax 4th Quartile	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	134		128		132		130	
with one or more adverse events	9	(6.7)	11	(8.6)	10	(7.6)	7	(5.4)
with no adverse event	125	(93.3)	117	(91.4)	122	(92.4)	123	(94.6)
with drug-related[†] adverse events	3	(2.2)	2	(1.6)	3	(2.3)	0	(0.0)
with serious adverse events	1	(0.7)	0	(0.0)	1	(0.8)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	1	(0.7)	0	(0.0)	1	(0.8)	0	(0.0)
discontinued due to a drug-related adverse event	1	(0.7)	0	(0.0)	1	(0.8)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
Cmax quartiles: Q1= 13100 (nM), median= 16850 (nM), Q3= 20500 (nM).
Cmax= Cmax (nM) at steady state.
Note: Raltegravir 1200 mg QD were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 68

Adverse Event Summary by Raltegravir AUC Quartile
Laboratory Adverse Events
Weeks 0-48

	Raltegravir 1200 mg QD							
	AUC 1st Quartile		AUC 2nd Quartile		AUC 3rd Quartile		AUC 4th Quartile	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	131		133		130		130	
with one or more adverse events	9	(6.9)	17	(12.8)	4	(3.1)	7	(5.4)
with no adverse event	122	(93.1)	116	(87.2)	126	(96.9)	123	(94.6)
with drug-related[†] adverse events	3	(2.3)	3	(2.3)	2	(1.5)	0	(0.0)
with serious adverse events	1	(0.8)	1	(0.8)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	2	(1.5)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	2	(1.5)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
AUC quartiles: Q1= 42250 (nM*h), median= 54600 (nM*h), Q3= 69000 (nM*h).
AUC= AUC0-24h (nM*h) at steady state.
Note: Raltegravir 1200 mg QD were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 69

Summary of Vital Signs
Weeks 0-48

Week	Raltegravir 1200 mg QD			Raltegravir 400 mg BID		
	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Diastolic Blood Pressure (mmHg)						
0	531	77.50		266	76.27	
1	507	77.46	-0.73 (8.91)	260	76.26	0.25 (8.10)
2	515	77.57	-1.04 (8.77)	252	76.36	0.37 (8.10)
4	527	77.46	-0.99 (8.79)	261	76.17	0.37 (9.02)
8	524	77.43	-0.45 (8.99)	260	76.25	0.73 (9.51)
16	513	77.47	0.40 (9.14)	257	76.35	0.95 (9.03)
24	510	77.53	-0.61 (9.40)	254	76.41	0.71 (9.30)
36	497	77.52	-0.03 (9.76)	249	76.47	0.86 (9.22)
48	492	77.59	0.01 (9.21)	247	76.51	1.25 (9.89)
Pulse Rate (beats/min)						
0	531	76.53		265	78.15	
1	507	76.62	0.18 (9.40)	259	78.02	0.62 (10.69)
2	515	76.37	0.40 (10.54)	251	77.91	0.44 (11.53)
4	527	76.37	0.24 (10.65)	260	77.83	-1.35 (11.04)
8	524	76.43	-0.29 (10.80)	259	77.87	-1.24 (11.90)
16	513	76.51	0.21 (11.57)	257	77.93	-1.40 (11.35)
24	511	76.63	-1.88 (11.24)	253	77.91	-2.34 (11.61)
36	498	76.68	-1.45 (11.43)	248	77.75	-2.94 (11.85)
48	493	76.76	-1.96 (11.19)	245	77.73	-3.16 (12.55)
Respiratory Rate (breaths/min)						
0	530	16.36		265	16.28	
1	500	16.35	-0.16 (1.98)	257	16.27	0.05 (1.89)
2	509	16.39	-0.13 (1.97)	249	16.33	0.15 (1.90)
4	522	16.36	-0.03 (2.06)	258	16.27	-0.01 (2.08)
8	518	16.36	0.03 (2.15)	257	16.26	0.12 (2.01)
16	507	16.38	-0.05 (2.28)	256	16.29	0.08 (2.57)
24	509	16.37	0.05 (2.31)	252	16.31	0.04 (2.32)
36	495	16.34	0.02 (2.30)	247	16.28	0.06 (2.40)
48	492	16.34	-0.10 (2.23)	246	16.26	0.31 (2.37)
Systolic Blood Pressure (mmHg)						
0	531	122.45		266	121.05	
1	507	122.37	-0.20 (10.84)	260	121.12	0.01 (11.72)
2	515	122.55	-0.84 (11.69)	252	121.23	0.58 (10.46)
4	527	122.38	-1.28 (11.82)	261	120.92	0.57 (11.91)
8	524	122.36	-0.46 (11.79)	260	121.10	0.80 (11.95)
16	513	122.42	1.40 (12.68)	257	121.23	1.46 (13.98)
24	510	122.53	-0.41 (12.92)	254	121.16	0.66 (13.22)
36	497	122.53	0.35 (13.12)	249	121.22	0.76 (12.41)
48	492	122.65	0.30 (13.60)	247	121.26	1.00 (13.37)

Summary of Vital Signs
Weeks 0-48

Week	Raltegravir 1200 mg QD			Raltegravir 400 mg BID		
	N	Baseline Mean	Mean Change[†](SD)	N	Baseline Mean	Mean Change[†](SD)
Temperature (C)						
0	531	36.53		265	36.52	
1	506	36.53	-0.04 (0.41)	258	36.53	-0.05 (0.39)
2	513	36.52	-0.02 (0.41)	250	36.52	0.02 (0.35)
4	527	36.52	-0.06 (0.48)	258	36.52	-0.05 (0.42)
8	523	36.53	-0.05 (0.42)	259	36.52	-0.02 (0.43)
16	511	36.53	-0.06 (0.42)	257	36.52	-0.04 (0.41)
24	510	36.53	-0.04 (0.43)	253	36.52	-0.04 (0.46)
36	498	36.52	-0.01 (0.45)	248	36.53	-0.03 (0.44)
48	493	36.52	-0.03 (0.44)	246	36.52	-0.03 (0.46)
Weight (kg)						
0	531	73.98		265	73.98	
48	485	74.00	1.97 (4.97)	243	74.00	2.17 (6.32)

[†]Change Scores are mean change from baseline and are based on the measurements of the subjects who were measured at baseline and the time point assessed.

Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

N = Number of patients subjects in the treatment group.

Data Source: [Ref. 5.3.5.1: P292V01]

Table 2.7.4: 70

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3066* Gender=[redacted] Race=[redacted] Age=28 Years, Rel Day of Last Recorded Dose of Study Medication=487											
P3066*	Treatment	169	Accidental overdose	1.02 Months	Severe	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3141* Gender=[redacted] Race=[redacted] Age=52 Years, Rel Day of Last Recorded Dose of Study Medication=476											
P3141*	Treatment	48	Accidental overdose	12 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3142* Gender=[redacted] Race=[redacted] Age=57 Years, Rel Day of Last Recorded Dose of Study Medication=422											
P3142*	Treatment	1	Accidental overdose	1 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3143* Gender=[redacted] Race=[redacted] Age=54 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3143*	Treatment	1	Accidental overdose	2 Days	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3144* Gender=[redacted] Race=[redacted] Age=33 Years, Rel Day of Last Recorded Dose of Study Medication=476											
P3144*	Treatment	298	Accidental overdose	12 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3145* Gender=[redacted] Race=[redacted] Age=32 Years, Rel Day of Last Recorded Dose of Study Medication=406											
P3145*	Treatment	9	Accidental overdose	2 Days	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3131* Gender=[redacted] Race=[redacted] Age=24 Years, Rel Day of Last Recorded Dose of Study Medication=392											
P3131*	Treatment	374	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3146* Gender=[redacted] Race=[redacted] Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=427											
P3146*	Treatment	58	Accidental overdose	4.29 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3147* Gender=[redacted] Race=[redacted] Age=23 Years, Rel Day of Last Recorded Dose of Study Medication=333											
P3147*	Treatment	18	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3148* Gender=[redacted] Race=[redacted] Age=48 Years, Rel Day of Last Recorded Dose of Study Medication=405											
P3148*	Treatment	2	Accidental overdose	23.98 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	2400.00 milligram
		360	Accidental overdose	15.98 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	1000.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	1200.00 milligram
		369	Accidental overdose	15.98 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	1000.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3149* Gender=[redacted] Race=[redacted], Age=32 Years, Rel Day of Last Recorded Dose of Study Medication=344											

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3149* Gender=[redacted] Race=[redacted], Age=32 Years, Rel Day of Last Recorded Dose of Study Medication=344											
P3149*	Treatment	2	Accidental overdose	1.86 Weeks	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3150* Gender=[redacted] Race=[redacted] Age=37 Years, Rel Day of Last Recorded Dose of Study Medication=495											
P3150*	Treatment	14	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram
		84	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 600.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3151* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=418											

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3151* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=418											
P3151*	Treatment	83	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3152* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=426											
P3152*	Treatment	68	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3153* Gender=[redacted] Race=[redacted] Age=40 Years, Rel Day of Last Recorded Dose of Study Medication=506											
P3153*	Treatment	69	Accidental overdose	1 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3154* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=403											
P3154*	Treatment	16	Accidental overdose	11 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 2400.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3155* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=418											
P3155*	Treatment	296	Accidental overdose	1 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3156* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=409											
P3156*	Treatment	312	Accidental overdose	2.08 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3157* Gender=[redacted] Race=[redacted] Age=35 Years, Rel Day of Last Recorded Dose of Study Medication=335											
P3157*	Treatment	82	Accidental overdose	2.02 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3091* Gender=[redacted] Race=[redacted] Age=39 Years, Rel Day of Last Recorded Dose of Study Medication=399											
P3091*	Treatment	57	Accidental overdose	11 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3021* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=253											
P3021*	Treatment	181	Accidental overdose	24 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 2400.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 1200 mg QD											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3021* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=253											
P3021*	Treatment	184	Accidental overdose	24 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	2400.00 milligram
		184	Accidental overdose	24 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	2400.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3158* Gender=[redacted] Race=[redacted] Age=29 Years, Rel Day of Last Recorded Dose of Study Medication=375											
P3158*	Treatment	68	Accidental overdose	24 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate	500.00 milligram
										placebo (unspecified)	0.00 milligram
										raltegravir	2400.00 milligram
Raltegravir 400 mg BID											

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3159* Gender=[redacted] Race=[redacted] Age=50 Years, Rel Day of Last Recorded Dose of Study Medication=372											
P3159*	Treatment	88	Accidental overdose	10 Minutes	Severe	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3160* Gender=[redacted] Race=[redacted] Age=34 Years, Rel Day of Last Recorded Dose of Study Medication=415											
P3160*	Treatment	248	Accidental overdose	1 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3161* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=41											
P3161*	Treatment	2	Accidental overdose	3 Days	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3161* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=41											
P3161*	Treatment	14	Accidental overdose	23.02 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	500.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3162* Gender=[redacted] Race=[redacted] Age=26 Years, Rel Day of Last Recorded Dose of Study Medication=462											
P3162*	Treatment	318	Accidental overdose	12 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3163* Gender=[redacted] Race=[redacted] Age=58 Years, Rel Day of Last Recorded Dose of Study Medication=487											
P3163*	Treatment	19	Accidental overdose	1 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3058* Gender=[redacted] Race=[redacted] Age=28 Years, Rel Day of Last Recorded Dose of Study Medication=384											
P3058*	Treatment	45	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3140* Gender=[redacted] Race=[redacted] Age=21 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3140*	Treatment	33	Accidental overdose	23 Hours	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 800.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3164* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3164*	Treatment	99	Accidental overdose	2 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3164* Gender=[redacted] Race=[redacted] Age=30 Years, Rel Day of Last Recorded Dose of Study Medication=420											
P3164*	Treatment	148	Accidental overdose	2.02 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3165* Gender=[redacted] Race=[redacted] Age=49 Years, Rel Day of Last Recorded Dose of Study Medication=413											
P3165*	Treatment	84	Accidental overdose	2.02 Minutes	Mild	N	N	None	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified) raltegravir	1000.00 milligram 0.00 milligram 1200.00 milligram
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3166* Gender=[redacted] Race=[redacted] Age=52 Years, Rel Day of Last Recorded Dose of Study Medication=480											
P3166*	Treatment	7	Accidental overdose	1.57 Weeks	Mild	N	N	N/A	Resolved	emtricitabine (+) tenofovir disoproxil fumarate placebo (unspecified)	1000.00 milligram 0.00 milligram

Listing of Subjects With Clinical Adverse Events - Report of ECI of Accidental Overdose without Adverse Effect
Weeks 0-48

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome	Therapy	Total Daily Dose
Raltegravir 400 mg BID											
Trial Number=0518-292, Site Number=[redacted] Subject ID=P3166* Gender=[redacted] Race=[redacted] Age=52 Years, Rel Day of Last Recorded Dose of Study Medication=480											
P3166*	Treatment	7	Accidental overdose	1.57 Weeks	Mild	N	N	N/A	Resolved	raltegravir	400.00 milligram

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.
Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Note: Raltegravir 1200 mg QD and raltegravir 400 mg BID were administered with TRUVADA™.

Data Source: [Ref. 5.3.5.1: P292V01]

[Ref. 5.4: 03QMY6] Wenning LA, Friedman EJ, Kost JT, Breidinger SA, Stek JE, Lasseter KC, et al. Lack of a Significant Drug Interaction between Raltegravir and Tenofovir. Antimicrob Agents Chemother 2008;52(9):3253-8.

[Ref. 5.4: 03QWGP] U.S.Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research (CDER), Center for Veterinary Medicine (CVM). Guidance for industry bioanalytical method validation.

[Ref. 5.4: 03RL3R] Zhang J, Kim TE, Kim J, Song I. Population PK and viral dynamic modeling of S/GSK1349572 in patients with HIV infection. 11th International Workshop on Clinical Pharmacology of HIV Therapy; 2010 Apr 7-9. Sorrento, Italy, 2010.

[Ref. 5.4: 03RL43] Memo to File from Wenning L, Hang Y, Luo W-L, Su J: Final Analysis MK-0518 PK/PD Associations of Once-Daily Versus Twice-Daily Raltegravir in Treatment-Naïve HIV-Infected Patients in a Phase III Study After 48 Weeks of Treatment (MK-0518 Protocol 071), 20[redacted].

[Ref. 5.4: 03RV3F] Van Luin M, Colbers A, van Ewijk-Beneken Kolmer EWJ, Verweij-van Wissen CPWGM, Schouwenberg B, Hoitsma A, et al. Drug-drug interactions between raltegravir and pravastatin in healthy volunteers. J Acquir Immune Defic Syndr 2010;55(1):82-6.

[Ref. 5.4: 03TSW9] MRL Modeling & Simulation Report: Development of a population pharmacokinetic model for the raltegravir component of Mk-0518b (lamivudine/raltegravir FDC tablet), projection of exposure in pediatric patients, and application of a PK-PD viral dynamics model to project efficacy of MK-0518B [redacted]-20[redacted].

[Ref. 5.4: 03TSXC] European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP): Guideline on bioanalytical method validation (EMEA/CHMP/EWP/192217/2009), 2011.

[Ref. 5.4: 03TTQ5] Funk GA, Fischer M, Joos B, Opravil M, Gunthard HF, Ledergerber B, et al. Quantification of in vivo replicative capacity of HIV-1 in different compartments of infected cells. J Acquir Immune Defic Syndr 2001;26(5):397-404.

[Ref. 5.4: 03Z7Q3] Rizk ML, Houle R, Chan GH, Hafey M, Rhee EG, Chu X. Raltegravir has a low propensity to cause clinical drug interactions through inhibition of major drug transporters: an in vitro evaluation. Antimicrob Agents Chemother. 2014 Mar;58(3):1294-301.

[Ref. 5.4: 04DLSJ] Dissolution Method Development Report for Raltegravir 600 mg Tablets, [redacted]-20[redacted].