Clinical trial results:
A Phase III 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

Summary

EudraCT number	2013-001939-47
Trial protocol	IT ES PT BE GB
Global end of trial date	19 December 2016

Results information

Result version number	v1 (current)
This version publication date	06 December 2017
First version publication date	06 December 2017

Trial information

Trial identification

Sponsor protocol code	0518-292

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02131233
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 December 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective was to evaluate the safety and efficacy of reformulated raltegravir (MK-0518) 1200 mg once daily in combination with TRUVADA™ versus raltegravir 400 mg twice daily in combination with TRUVADA™ in HIV-1 infected, treatment-naive participants. The primary hypothesis being tested is that reformulated raltegravir 1200 mg once-daily is non-inferior to raltegravir 400 mg twice-daily, each in combination therapy with TRUVADA™, as assessed by the proportion of participants achieving HIV-1 ribonucleic acid (RNA) <40 copies/mL at Week 48.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 May 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 16
Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Chile: 25
Country: Number of subjects enrolled	Colombia: 19
Country: Number of subjects enrolled	France: 35
Country: Number of subjects enrolled	Germany: 54
Country: Number of subjects enrolled	Guatemala: 35
Country: Number of subjects enrolled	Israel: 22
Country: Number of subjects enrolled	Italy: 44
Country: Number of subjects enrolled	Malaysia: 26
Country: Number of subjects enrolled	Peru: 8
Country: Number of subjects enrolled	Philippines: 10
Country: Number of subjects enrolled	Portugal: 29
Country: Number of subjects enrolled	Russian Federation: 40
Country: Number of subjects enrolled	South Africa: 57

Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	Taiwan: 14
Country: Number of subjects enrolled	Thailand: 52
Country: Number of subjects enrolled	United Kingdom: 19
Country: Number of subjects enrolled	United States: 175
Worldwide total number of subjects	802
EEA total number of subjects	236

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	795
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Males and females 18 years of age or older who were HIV-1 positive and naïve to antiretroviral therapy (ART) were enrolled in this trial.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Reformulated Raltegravir

Arm description:

Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks.

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

Dosage and administration details:

1200 mg (2x 600 mg tablets) orally once daily

Investigational medicinal product name	TRUVADA™
Investigational medicinal product code	
Other name	Emtricitabine /tenofovir disoproxil fumarate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/300 mg tablet administered once daily with food (open-label)

Arm title	Raltegravir

Arm description:

Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks.

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

Dosage and administration details:

400 mg tablet orally twice daily

Investigational medicinal product name	TRUVADA™
Investigational medicinal product code	
Other name	Emtricitabine /tenofovir disoproxil fumarate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/300 mg tablet administered once daily with food (open-label)

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

Dosage and administration details:

Two tablets orally twice daily

Number of subjects in period 1	Reformulated Raltegravir	Raltegravir
Started	533	269
Completed	531	266
Not completed	2	3
Not Treated	2	3

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Reformulated Raltegravir

Arm description:

Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally
once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks.

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

Dosage and administration details:

1200 mg (2x 600 mg tablets) orally once daily

Investigational medicinal product name	TRUVADA™
Investigational medicinal product code	
Other name	Emtricitabine /tenofovir disoproxil fumarate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/300 mg tablet administered once daily with food (open-label)

Arm title	Raltegravir

Arm description:

Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks.

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

Dosage and administration details:

400 mg tablet orally twice daily

Investigational medicinal product name	TRUVADA™
Investigational medicinal product code	
Other name	Emtricitabine /tenofovir disoproxil fumarate
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200/300 mg tablet administered once daily with food (open-label)

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

Dosage and administration details:

Two tablets orally twice daily

Notes:

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

Justification: Period 1, enrolled participants, was not the baseline period. Instead Period 2, treated participants, was assigned as the baseline period.

Number of subjects in period 2[2]	Reformulated Raltegravir	Raltegravir
Started	531	266
Completed	467	227
Not completed	64	39
Adverse event, serious fatal	-	1
Physician decision	7	-
Consent withdrawn by subject	18	11
Adverse event, non-fatal	7	6
Non-Compliance With Study Drug	8	5
Pregnancy	4	-

Lost to follow-up	14	13
Lack of efficacy	6	3

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The worldwide number of enrolled participants, was not the baseline period. Instead treated participants, was assigned as the baseline period.

Baseline characteristics

Reporting groups	
Reporting group title	Reformulated Raltegravir
Reporting group description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks.	
Reporting group title	Raltegravir
Reporting group description:	
Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks.	

Reporting group values	Reformulated Raltegravir	Raltegravir	Total
Number of subjects	531	266	797
Age Categorical			
Treated Participants			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	527	263	790
From 65-84 years	4	3	7
85 years and over	0	0	0
Age Continuous			
Treated Participants			
Units: years			
arithmetic mean	35.4	36.9	
standard deviation	± 10.3	± 11.0	-
Gender Categorical			
Treated Participants			
Units: Subjects			
Female	91	32	123
Male	440	234	674

Subject analysis sets	
Subject analysis set title	Reformulated Raltegravir
Subject analysis set type	Safety analysis
Subject analysis set description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks	
Subject analysis set title	Raltegravir
Subject analysis set type	Safety analysis

Subject analysis set description:

Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks

Reporting group values	Reformulated Raltegravir	Raltegravir	
Number of subjects	531	266	
Age Categorical			
Treated Participants			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	527	263	
From 65-84 years	4	3	
85 years and over	0	0	
Age Continuous			
Treated Participants			
Units: years			
arithmetic mean	35.4	36.9	
standard deviation	± 10.3	± 11.0	
Gender Categorical			
Treated Participants			
Units: Subjects			
Female	91	32	
Male	440	234	

End points

End points reporting groups

Reporting group title	Reformulated Raltegravir
Reporting group description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks.	
Reporting group title	Raltegravir
Reporting group description:	
Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks.	
Reporting group title	Reformulated Raltegravir
Reporting group description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks.	
Reporting group title	Raltegravir
Reporting group description:	
Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks.	
Subject analysis set title	Reformulated Raltegravir
Subject analysis set type	Safety analysis
Subject analysis set description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks	
Subject analysis set title	Raltegravir
Subject analysis set type	Safety analysis
Subject analysis set description:	
Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks	

Primary: Percentage of Participants Achieving <40 copies/mL Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) at Week 48

End point title	Percentage of Participants Achieving <40 copies/mL Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) at Week 48
End point description:	
From blood samples collected at week 48, HIV-1 RNA levels were determined by the Abbott RealTime HIV-1 Assay, which has a limit of reliable quantification (LoQ) of 40 copies/mL. The NC=F approach as defined by FDA "snapshot" approach was used as the primary approach to analysis where all missing data were treated as failures regardless of the reason. The population analyzed was all randomized participants who received at least one dose of study treatment.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (confidence interval 95%)	88.9 (85.9 to 91.4)	88.3 (83.9 to 91.9)		

Statistical analyses

Statistical analysis title	Reformulated Raltegravir minus Raltegravir

Statistical analysis description:

The 95% Confidence Interval (CI) 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).

Comparison groups	Reformulated Raltegravir v Raltegravir
Number of subjects included in analysis	797
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Estimated Difference
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.204
upper limit	5.223

Notes:

[1] - Reformulated Raltegravir is concluded non-inferior to Raltegravir if the lower bound of the 95% CI for the difference in percent response is above -10 percentage points.

Secondary: Percentage of Participants Achieving <40 copies/mL HIV RNA at Week 96

End point title	Percentage of Participants Achieving <40 copies/mL HIV RNA at Week 96

End point description:

From blood samples collected at week 96, HIV-1 RNA levels were determined by the Abbott RealTime HIV-1 Assay, which has a limit of reliable quantification (LoQ) of 40 copies/mL. The NC=F approach as defined by FDA "snapshot" approach was used as the primary approach to analysis where all missing data were treated as failures regardless of the reason. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Week 96

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	81.5	80.1		

Statistical analyses

Statistical analysis title	Reformulated Raltegravir minus Raltegravir

Statistical analysis description:

The 95% Confidence Interval (CI) 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).

Comparison groups	Reformulated Raltegravir v Raltegravir
Number of subjects included in analysis	797
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Estimated Difference
Point estimate	1.449
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.41
upper limit	7.308

Notes:

[2] - Reformulated Raltegravir is concluded noninferior to Raltegravir if the lower bound of the 95% CI for the difference in percent response is above -10 percentage points.

Secondary: Change from Baseline in Cluster of Differentiation 4 (CD4) Cell Count at Week 48

End point title	Change from Baseline in Cluster of Differentiation 4 (CD4) Cell Count at Week 48

End point description:

CD4 cells were counted from blood collected at baseline and week 48, and the change from baseline determined from week 48 minus baseline values.The population analyzed was all randomized participants who received at least one dose of study treatment and have baseline data. The Observed Failure (OF) approach to handling missing values assumed baseline-carry-forward for all failures, and excluded other missing values.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	499	251		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	232.0 (214.6 to 249.4)	234.1 (212.8 to 255.3)		

Statistical analyses

Statistical analysis title	Reformulated Raltegravir minus Raltegravir
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Reformulated Raltegravir v Raltegravir
Number of subjects included in analysis	750
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference (Final Values)
Point estimate	-2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.9
upper limit	26.7

Secondary: Change from Baseline in CD4 Cell Count at Week 96

End point title	Change from Baseline in CD4 Cell Count at Week 96
End point description:	
CD4 cells were counted from blood collected at baseline and week 96, and the change from baseline determined from week 96 minus baseline values. The population analyzed was all randomized participants who received at least one dose of study treatment and have baseline data. The Observed Failure (OF) approach to handling missing values assumed baseline-carry-forward for all failures, and excluded other missing values.	
End point type	Secondary
End point timeframe:	
Baseline and Week 96	

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	482	235		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	261.6 (242.9 to 280.3)	262.2 (236.4 to 288.0)		

Statistical analyses

Statistical analysis title	Reformulated Raltegravir minus Raltegravir
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Reformulated Raltegravir v Raltegravir
Number of subjects included in analysis	717
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean Difference (Final Values)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.8
upper limit	31.6

Secondary: Percentage of Participants with an Adverse Event (AE) at Week 48

End point title	Percentage of Participants with an Adverse Event (AE) at Week 48

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	83.2	88.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an AE after 96 weeks of Treatment

End point title	Percentage of Participants with an AE after 96 weeks of Treatment

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 98 (96 weeks of treatment + 2 weeks of follow up)

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	90.8	94.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Drug-Related AE at Week 48

End point title	Percentage of Participants with a Drug-Related AE at Week 48

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether
or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. An investigator who is a qualified physician evaluated whether or not an AE was drug-related. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	25.0	27.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Drug-Related AE after 96 weeks of Treatment

End point title	Percentage of Participants with a Drug-Related AE after 96 weeks of Treatment

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether
or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor’s product, is also an AE. An investigator who is a qualified physician evaluated whether or not an AE was drug-related. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 98 (96 weeks of treatment + 2 weeks of follow up)

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	26.4	28.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Serious Adverse Event (SAE) at Week 48

End point title	Percentage of Participants with a Serious Adverse Event (SAE) at Week 48

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that does the following: results in death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing inpatient hospitalization; is a congenital anomaly/birth defect; is a cancer; is associated with an overdose; is another important medical event. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	6.2	9.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with SAE after 96 weeks of Treatment

End point title	Percentage of Participants with SAE after 96 weeks of Treatment

End point description:

A SAE is any AE occurring at any dose or during any use of Sponsor's product that does the following: results in death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing inpatient hospitalization; is a congenital anomaly/birth defect; is a cancer; is associated with an overdose; is another important medical event. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 98 (96 weeks of treatment + 2 weeks of follow up)

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	9.6	15.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Serious and Drug-Related AE at Week 48

End point title	Percentage of Participants with a Serious and Drug-Related AE at Week 48

End point description:

A SAE is any AE occurring at any dose or during any use of Sponsor's product that does the following: results in death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing inpatient hospitalization; is a congenital anomaly/birth defect; is a cancer; is associated with an overdose; is another important medical event. An investigator who is a qualified physician evaluated whether or not a SAE is drug-related.The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	0.2	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Serious and Drug-Related AE after 96 weeks of Treatment

End point title	Percentage of Participants with a Serious and Drug-Related AE after 96 weeks of Treatment

End point description:

A SAE is any AE occurring at any dose or during any use of Sponsor's product that does the following: results in death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing inpatient hospitalization; is a congenital anomaly/birth defect; is a cancer; is associated with an overdose; is another important medical event. An investigator who is a qualified physician evaluated whether or not a SAE is drug-related. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 98 (96 weeks of treatment + 2 weeks of follow up)

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	0.2	0.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Discontinued from Drug Therapy Due to an AE at Week 48

End point title	Percentage of Participants Who Discontinued from Drug Therapy Due to an AE at Week 48

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	1.1	2.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Discontinued from Drug Therapy Due to an AE up to Week 96

End point title	Percentage of Participants Who Discontinued from Drug Therapy Due to an AE up to Week 96

End point description:

An AE is defined as any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product or protocol specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The population analyzed was all randomized participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 96

End point values	Reformulated Raltegravir	Raltegravir		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	531	266		
Units: Percentage of participants				
number (not applicable)	1.3	2.3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to Week 98 (96 weeks of treatment + 2 weeks of follow up)	
Adverse event reporting additional description:	
All randomized participants who received at least one dose of study treatment.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups	
Reporting group title	Raltegravir 1200 mg QD + Truvada
Reporting group description:	
Reformulated raltegravir 1200 mg (2x 600 mg tablets) orally once daily plus placebo to raltegravir 1 tablet orally twice daily plus TRUVADA™ orally once daily for 96 weeks	
Reporting group title	Raltegravir 400 mg BID + Truvada
Reporting group description:	
Raltegravir 400 mg tablet orally twice daily plus placebo to reformulated raltegravir 2 tablets orally once daily plus TRUVADA™ orally once daily for 96 weeks	

Serious adverse events	Raltegravir 1200 mg QD + Truvada	Raltegravir 400 mg BID + Truvada	
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 531 (9.60%)	42 / 266 (15.79%)	
number of deaths (all causes)	2	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of salivary gland			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal squamous cell carcinoma			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anogenital warts			
subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Basal cell carcinoma			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer in situ			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burkitt's lymphoma			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunoblastic lymphoma			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Drug ineffective			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcoholism			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	4 / 531 (0.75%)	2 / 266 (0.75%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emotional distress			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	2 / 531 (0.38%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			

subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			

subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Cerebrovascular accident			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Enteritis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	1 / 531 (0.19%)	2 / 266 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal perforation			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	2 / 531 (0.38%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			

subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone pain			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteochondrosis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired immunodeficiency syndrome			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anal abscess			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 531 (0.19%)	2 / 266 (0.75%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis perforated			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral toxoplasmosis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Dengue fever			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphogranuloma venereum			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis tuberculous			

subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasmodium vivax infection			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis chlamydial			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis infectious			

subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 531 (0.19%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 531 (0.19%)	0 / 266 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	0 / 531 (0.00%)	1 / 266 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Raltegravir 1200 mg QD + Truvada	Raltegravir 400 mg BID + Truvada	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	375 / 531 (70.62%)	184 / 266 (69.17%)	
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	26 / 531 (4.90%)	18 / 266 (6.77%)	
occurrences (all)	31	19	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	29 / 531 (5.46%)	17 / 266 (6.39%)	
occurrences (all)	35	25	
Nervous system disorders			
Dizziness			
subjects affected / exposed	39 / 531 (7.34%)	19 / 266 (7.14%)	
occurrences (all)	46	20	
Headache			
subjects affected / exposed	84 / 531 (15.82%)	37 / 266 (13.91%)	
occurrences (all)	106	45	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	40 / 531 (7.53%)	17 / 266 (6.39%)	
occurrences (all)	44	19	
Influenza like illness			
subjects affected / exposed	14 / 531 (2.64%)	14 / 266 (5.26%)	
occurrences (all)	16	19	
Pyrexia			
subjects affected / exposed	26 / 531 (4.90%)	15 / 266 (5.64%)	
occurrences (all)	30	16	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	46 / 531 (8.66%)	12 / 266 (4.51%)	
occurrences (all)	57	15	
Diarrhoea			
subjects affected / exposed	71 / 531 (13.37%)	34 / 266 (12.78%)	
occurrences (all)	82	42	
Nausea			
subjects affected / exposed	72 / 531 (13.56%)	34 / 266 (12.78%)	
occurrences (all)	88	38	
Vomiting			
subjects affected / exposed	42 / 531 (7.91%)	20 / 266 (7.52%)	
occurrences (all)	45	24	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	40 / 531 (7.53%)	17 / 266 (6.39%)	
occurrences (all)	48	19	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	18 / 531 (3.39%)	17 / 266 (6.39%)	
occurrences (all)	21	18	
Rash			
subjects affected / exposed	30 / 531 (5.65%)	13 / 266 (4.89%)	
occurrences (all)	35	14	
Psychiatric disorders			
Depression			
subjects affected / exposed	17 / 531 (3.20%)	15 / 266 (5.64%)	
occurrences (all)	19	17	
Insomnia			
subjects affected / exposed	31 / 531 (5.84%)	18 / 266 (6.77%)	
occurrences (all)	31	18	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	27 / 531 (5.08%)	7 / 266 (2.63%)	
occurrences (all)	32	9	
Back pain			

subjects affected / exposed	39 / 531 (7.34%)	14 / 266 (5.26%)	
occurrences (all)	47	15	
Infections and infestations			
Bronchitis			
subjects affected / exposed	29 / 531 (5.46%)	14 / 266 (5.26%)	
occurrences (all)	32	16	
Influenza			
subjects affected / exposed	31 / 531 (5.84%)	18 / 266 (6.77%)	
occurrences (all)	41	22	
Nasopharyngitis			
subjects affected / exposed	65 / 531 (12.24%)	26 / 266 (9.77%)	
occurrences (all)	88	35	
Syphilis			
subjects affected / exposed	28 / 531 (5.27%)	19 / 266 (7.14%)	
occurrences (all)	30	21	
Upper respiratory tract infection			
subjects affected / exposed	67 / 531 (12.62%)	27 / 266 (10.15%)	
occurrences (all)	90	37	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2014	Amendment 1 was to extend the screening period time as well as to modify the inclusion criteria regarding birth control to allow local regulations to be followed. In addition there was additional text added to define antiretroviral therapy to be used during the trial; define complete physical examination; define type of meal consumed before or after dose of study medication; update to emergency call center information; update regarding unblended trial statistician; additional details for local discard requirements.
08 September 2015	Amendment 2 was completed to switch from electronic to paper study diaries.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported