Clinical trial results:
A Phase III study to demonstrate the antiviral activity and safety of dolutegravir in HIV-1 infected adult subjects with treatment failure on an integrase inhibitor containing regimen.

Summary

EudraCT number	2009-017951-87
Trial protocol	BE PT IT ES
Global end of trial date	25 May 2015

Results information

Result version number	v1 (current)
This version publication date	12 May 2016
First version publication date	12 May 2016

Trial information

Trial identification

Sponsor protocol code	112574

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,
Scientific contact	GSK Response Center, GlaxoSmithKline, +1 8664357343,

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?	
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 August 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 May 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this trial is to assess the antiviral activity and safety of a dolutegravir (DTG) containing regimen in HIV-1 infected, antiretroviral therapy (ART)-experienced adults with current or historical failure on an integrase inhibitor (INI) containing regimen. The study will assess DTG 50mg twice daily administered initially with the current failing ART regimen but then with an optimised background ART regimen (OBR) after Day 7. The first analyses will be conducted after the last subject enrolled has completed 24 weeks. Subjects may remain on study after Week 24.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 May 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Portugal: 6
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	United States: 99
Worldwide total number of subjects	183
EEA total number of subjects	81

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	179
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants (par.) having documented Human immunodeficiency virus type 1 (HIV-1) infection with a plasma HIV-1 Ribonucleic acid(RNA) >=500 copies per milliliter (c/mL) at Screening, Antiretroviral therapy (ART)-experienced and on stable ART for at least one month prior to Screening were enrolled

Pre-assignment

Screening details:

A total of 139 par. were screen failures and 183 par. entered the single arm, open-label study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Dolutegravir 50 mg BID

Arm description:

Participants received dolutegravir (DTG) 50 milligrams (mg) twice a day (BID).

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

Dosage and administration details:

1 X 50mg tablet twice daily, Tablet for oral use

Number of subjects in period 1	Dolutegravir 50 mg BID
Started	183
Completed	126
Not completed	57
Physician decision	2
Consent withdrawn by subject	7
Adverse event, non-fatal	7
Lost to follow-up	7
Lack of efficacy	27
Protocol deviation	7

Baseline characteristics

Reporting groups	
Reporting group title	Overall Study

Reporting group description: -

Reporting group values	Overall Study	Total	
Number of subjects	183	183	
Age categorical Units: Subjects			
Age continuous Units: years			
median	48		
full range (min-max)	19 to 67	-	
Gender categorical Units: Subjects			
Female	42	42	
Male	141	141	
Race Units: Subjects			
African American/African Heritage	49	49	
American Indian or Alaska Native and White	1	1	
Asian-Central/South Asian Heritage	1	1	
White	130	130	
White and African American/African Heritage	2	2	

End points

End points reporting groups

Reporting group title	Dolutegravir 50 mg BID
Reporting group description:	
Participants received dolutegravir (DTG) 50 milligrams (mg) twice a day (BID).	

Primary: Mean change from Baseline in Plasma HIV-1 RNA at Day 8

End point title	Mean change from Baseline in Plasma HIV-1 RNA at Day 8[1]
End point description:	
Mean change from Baseline in Plasma Human Immunodeficiency Virus-1 (HIV-1) Ribonucleic Acid (RNA) at Day 8 was calculated as the Day 8 value minus the Baseline value. The last observation was carried forward if a participant had missed the Day 8 visit. The Baseline observation was carried forward if a participant had discontinued the treatment before Day 8. Blood samples for assessment of HIV-1 RNA levels were collected at Baseline and Day 8. The P-value (< 0.001) was derived by the null hypothesis testing of no change from Baseline in HIV-1 RNA at Day 8 at the two-sided 5% significance level using a single sample 2 sided, t-test. Change from baseline (-1.432) and 2 sided 95% confidence interval (-1.520 to -1.343) was calculated using T distribution. Intent-to-Treat-Exposed (ITT-E) Population is defined as all participants who received at least one dose of study drug. Only participants who had Day 8 observations were considered for analysis.	
End point type	Primary
End point timeframe:	
Baseline and Day 8	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	182[2]			
Units: log10 copies/milliliter (mL)				
arithmetic mean (standard deviation)	-1.432 (± 0.607)			

Notes:

[2] - Intent-to-treat-Exposed Population. One participant did not have a Day 8 visit.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with HIV-1 RNA less than 50 copies (c)/mL at Week 24

End point title	Number of participants with HIV-1 RNA less than 50 copies (c)/mL at Week 24[3]
End point description:	
The number of par. who had viral load <50 c/mL at Week 24 based on the Food and Drug Administration's Snapshot algorithm was assessed. This algorithm treats all par. without HIV-1 RNA data at the visit of interest (VOI [due to missing data/discontinuation of investigational product prior to the visit window]) as nonresponders, as well as par. who switched their concomitant antiretroviral (ART) prior to the VOI as follows: background ART substitutions not permitted per protocol; background ART substitutions permitted per protocol, however the decision to switch was not documented as being	

before or at the first on-treatment visit after switching to optimized background regimen (i.e., Week 4) where HIV-1 RNA was assessed. Otherwise, virologic success/failure was to be determined by the last available HIV-1 RNA assessment while the par. was on treatment within the VOI analysis window. The percentage of par. with HIV-1 RNA <50 c/mL at week 24 was 69% with 2 sided 95% CI as 62% to 76%.

End point type	Primary

End point timeframe:

Week 24

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[4]			
Units: participants				
number (not applicable)	126			

Notes:

[4] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with HIV-1 RNA less than 50 copies(c)/mL at Week 48

End point title	Number of participants with HIV-1 RNA less than 50 copies(c)/mL at Week 48[5]

End point description:

The number of participants who had viral load <50 c/mL at Week 48 based on the Food and Drug Administration's Snapshot algorithm was assessed. This algorithm treats all participants without HIV-1 RNA data at the VOI (due to missing data/discontinuation of investigational product prior to the visit window) as non responders, as well as participants who switched their concomitant ART prior to the VOI as follows: background ART substitutions not permitted per protocol; background ART substitutions permitted per protocol, however the decision to switch was not documented as being before or at the first on-treatment visit after switching to optimized background regimen (i.e., Week 4) where HIV-1 RNA was assessed. Otherwise, virologic success/failure was to be determined by the last available HIV-1 RNA assessment while the participant was on treatment within the VOI analysis window. The percentage of participants with HIV-1 RNA <50 c/mL at Week 48 was 63% with 2 sided 95% CI as 56% to 70%.

End point type	Primary

End point timeframe:

Week 48

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[6]			
Units: participants				
number (not applicable)	116			

Notes:

[6] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any Adverse Event (AE) or any serious adverse event (SAE)

End point title	Number of participants with any Adverse Event (AE) or any serious adverse event (SAE)[7]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is an event of possible drug-induced liver injury.

End point type	Primary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[8]			
Units: participants				
number (not applicable)				
Any AE	169			
Any SAE	46			

Notes:

[8] - Safety Population: all participants who received at least one dose of study drug.

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with Adverse Events of the indicated severity, per the Division of Acquired Immune Deficiency Syndrome (DAIDS) grading scale

End point title	Number of participants with Adverse Events of the indicated severity, per the Division of Acquired Immune Deficiency Syndrome (DAIDS) grading scale[9]

End point description:

An AE is defined as any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the

medicinal product. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a medicinal product. An SAE is defined as any untoward medical occurrence that, at any dose, results in death, is life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect, or is an event of possible drug-induced liver injury. AE/SAE severity was graded according to the DAIDS grading scale. The DAIDS displays events as Grades 1-4 based on this general guideline: Grade (G) 1, mild; G2, moderate; G3, severe; G4, potentially life threatening.

End point type	Primary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[10]			
Units: participants				
number (not applicable)				
Grade 1	45			
Grade 2	64			
Grade 3	44			
Grade 4	16			

Notes:

[10] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the maximum post-Baseline-emergent clinical chemistry toxicities of the indicated grade

End point title	Number of participants with the maximum post-Baseline-emergent clinical chemistry toxicities of the indicated grade[11]

End point description:

The severity of clinical chemistry toxicities was graded according to the DAIDS toxicity scale. The DAIDS displays events as Grades 1-5 based on this general guideline: Grade (G) 1, mild; G2, moderate; G3, severe; G4, life threatening; G5, death related to toxicity.

End point type	Primary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[12]			
Units: participants				
number (not applicable)				
Grade 1	49			
Grade 2	67			
Grade 3	43			
Grade 4	16			

Notes:

[12] - Safety Population

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with the maximum post-Baseline-emergent hematology toxicities of the indicated grade

End point title	Number of participants with the maximum post-Baseline-emergent hematology toxicities of the indicated grade[13]

End point description:

The severity of hematology toxicities was graded according to the DAIDS. The DAIDS displays events as Grades 1-5 based on this general guideline: Grade (G) 1, mild; G2, moderate; G3, severe; G4, life threatening; G5, death related to toxicity.

End point type	Primary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There are no statistical data to report.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[14]			
Units: Participants				
number (not applicable)				
Grade 1	31			
Grade 2	15			
Grade 3	4			
Grade 4	2			

Notes:

[14] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with plasma HIV-1 RNA less than 400 and 50 copies/mL at Baseline; Day 8; and Weeks 4, 8, 12, 16, 24, 32, 40, and 48

End point title	Number of participants with plasma HIV-1 RNA less than 400 and 50 copies/mL at Baseline; Day 8; and Weeks 4, 8, 12, 16, 24, 32, 40, and 48

End point description:

The number of participants with plasma HIV-1 RNA less than 400 and 50 copies (c)/mL at Baseline; Day 8; and Weeks 4, 8, 12, 16, 24, 32, 40 and 48 based on the Food and Drug Administration's Snapshot algorithm was assessed. This algorithm treats all participants without HIV-1 RNA data at the visit of interest (VOI [due to missing data/discontinuation of investigational product prior to the visit window]) as nonresponders, as well as participants who switched their concomitant antiretroviral (ART) prior to the VOI as follows: background ART substitutions not permitted per protocol; background ART substitutions permitted per protocol, however the decision to switch was not documented as being before or at the first on-treatment visit after switching to optimized background regimen (i.e., Week 4) where HIV-1 RNA was assessed. Otherwise, virologic success/failure was to be determined by the last available HIV-1 RNA assessment while the par. was on treatment within the VOI analysis window

End point type	Secondary

End point timeframe:

Baseline; Day 8; and Weeks 4, 8, 12, 16, 24, 32, 40, and 48

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[15]			
Units: participants				
number (not applicable)				
HIV-1 RNA <50 c/mL, Baseline	1			
HIV-1 RNA <50 c/mL, Day 8	28			
HIV-1 RNA <50 c/mL, Week 4	98			
HIV-1 RNA <50 c/mL, Week 8	112			
HIV-1 RNA <50 c/mL, Week 12	116			
HIV-1 RNA <50 c/mL, Week 16	116			
HIV-1 RNA <50 c/mL, Week 24	126			
HIV-1 RNA <50 c/mL, Week 32	117			
HIV-1 RNA <50 c/mL, Week 40	108			
HIV-1 RNA <50 c/mL, Week 48	116			
HIV-1 RNA <400 c/mL, Baseline	8			
HIV-1 RNA <400 c/mL, Day 8	82			
HIV-1 RNA <400 c/mL, Week 4	145			
HIV-1 RNA <400 c/mL, Week 8	146			
HIV-1 RNA <400 c/mL, Week 12	142			
HIV-1 RNA <400 c/mL, Week 16	139			
HIV-1 RNA <400 c/mL, Week 24	135			
HIV-1 RNA <400 c/mL, Week 32	127			
HIV-1 RNA <400 c/mL, Week 40	119			
HIV-1 RNA <400 c/mL, Week 48	125			

Notes:

[15] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with plasma HIV-1 RNA less than 400 and 50

copies/mL from Week 48 every 12 weeks up to study completion	
End point title	Number of participants with plasma HIV-1 RNA less than 400 and 50 copies/mL from Week 48 every 12 weeks up to study completion

End point description:

The number of participants with plasma HIV-1 RNA less than 400 and 50 copies (c)/mL was assessed at Weeks 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168 and 180 using data of observed cases. Only those participants available at the specified time points were analyzed (represented by n=X in the category titles). Intention to treat-Exposed (ITT-E) population was defined as only those participants with data available at the indicated time points were considered for analysis (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT-E Population.

End point type	Secondary

End point timeframe:

From Week 48 every 12 weeks up to study completion.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[16]			
Units: Participants				
number (not applicable)				
HIV-1 RNA <50 c/mL, Week 48, n =146	121			
HIV-1 RNA <50 c/mL, Week 60, n=142	110			
HIV-1 RNA <50 c/mL, Week 72, n=138	116			
HIV-1 RNA <50 c/mL, Week 84, n=138	108			
HIV-1 RNA <50 c/mL, Week 96, n=120	101			
HIV-1 RNA <50 c/mL, Week 108, n=98	81			
HIV-1 RNA <50 c/mL, Week 120, n=82	72			
HIV-1 RNA <50 c/mL, Week 132, n=61	49			
HIV-1 RNA <50 c/mL, Week 144, n=45	37			
HIV-1 RNA <50 c/mL, Week 156, n=32	28			
HIV-1 RNA <50 c/mL, Week 168, n=24	20			
HIV-1 RNA <50 c/mL, Week 180, n=6	4			
HIV-1 RNA <400 c/mL, Week 48, n=146	134			
HIV-1 RNA <400 c/mL, Week 60, n=142	131			
HIV-1 RNA <400 c/mL, Week 72, n=138	130			
HIV-1 RNA <400 c/mL, Week 84, n=138	127			
HIV-1 RNA <400 c/mL, Week 96, n=120	111			
HIV-1 RNA <400 c/mL, Week 108, n=98	92			
HIV-1 RNA <400 c/mL, Week 120, n=82	80			
HIV-1 RNA <400 c/mL, Week 132, n=61	59			
HIV-1 RNA <400 c/mL, Week 144, n=45	44			
HIV-1 RNA <400 c/mL, Week 156, n=32	31			
HIV-1 RNA <400 c/mL, Week 168, n=24	23			
HIV-1 RNA <400 c/mL, Week 180, n=6	5			

Notes:

[16] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in plasma HIV-1 RNA at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and from Week 48 every 12 weeks up to study completion

End point title	Mean change from Baseline in plasma HIV-1 RNA at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and from Week 48 every 12 weeks up to study completion

End point description:

Mean change from Baseline in plasma HIV-1 RNA was assessed at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, 48 , 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, and 180 using data of the observed cases. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Intention to treat-Exposed (ITT-E) population was defined as only those participants with data available at the indicated time points were considered for analysis (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT-E Population.

End point type	Secondary

End point timeframe:

Baseline; Day 8; Weeks 4, 8, 12, 16, 24, 32, 40, and From Week 48 Every 12 Weeks up to Study completion (Up to Week 180)

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[17]			
Units: Log10 copies/mL				
arithmetic mean (standard deviation)				
Day 8, n=182	-1.432 (± 0.607)			
Week 4, n=180	-2.088 (± 0.885)			
Week 8, n=179	-2.101 (± 0.987)			
Week 12, n=174	-2.113 (± 1.069)			
Week 16, n=165	-2.216 (± 1.005)			
Week 24, n=164	-2.211 (± 1.023)			
Week 32, n=146	-2.373 (± 0.926)			
Week 40, n=144	-2.301 (± 0.955)			
Week 48, n=146	-2.321 (± 0.981)			
Week 60, n=142	-2.356 (± 0.928)			
Week 72, n=138	-2.39 (± 0.941)			
Week 84, n=138	-2.311 (± 0.996)			
Week 96, n=120	-2.346 (± 1.008)			
Week 108, n=98	-2.394 (± 0.966)			
Week 120, n=82	-2.515 (± 0.904)			

Week 132, n=61	-2.456 (± 0.988)			
Week 144, n=45	-2.585 (± 0.983)			
Week 156, n=32	-2.595 (± 1.009)			
Week 168, n=24	-2.719 (± 0.898)			
Week 180, n=6	-2.425 (± 1.557)			

Notes:

[17] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values for CD4+ cell counts at Baseline, Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and 48 and for CD8+ cell counts at Baseline and Weeks 4, 12, 24, and 48

End point title	Absolute values for CD4+ cell counts at Baseline, Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and 48 and for CD8+ cell counts at Baseline and Weeks 4, 12, 24, and 48

End point description:

Absolute values for CD4+ cell counts were assessed at Baseline, Day 8 and Weeks 4, 8, 12, 16, and 24, and absolute values for CD8+ cell counts were assessed at Baseline and Weeks 4, 12, 24, and 48. Only those participants with data available at the indicated time points were considered for analysis (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT-E Population.

End point type	Secondary

End point timeframe:

Baseline, Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and 48

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[18]			
Units: Cells per millimeters cubed (cells/mm^3)				
median (inter-quartile range (Q1-Q3))				
CD4+, Baseline, n=183	140 (40 to 330)			
CD4+, Day 8, n=181	170 (60 to 350)			
CD4+, Week 4, n=178	185 (80 to 350)			
CD4+, Week 8, n=178	210 (100 to 350)			
CD4+, Week 12, n=171	210 (110 to 360)			
CD4+, Week 16, n=165	210 (130 to 400)			
CD4+, Week 24, n=163	250 (130 to 420)			

CD4+, Week 32, n=147	270 (170 to 440)			
CD4+, Week 40, n=143	290 (200 to 440)			
CD4+, Week 48, n=145	310 (200 to 450)			
CD8+, Week 4, n=181	860 (540 to 1220)			
CD8+, Week 4, n=176	970 (655 to 1405)			
CD8+, Week 12, n=170	1015 (730 to 1460)			
CD8+, Week 24, n=154	1020 (690 to 1460)			
CD8+, Week 48, n=140	1000 (720 to 1380)			

Notes:

[18] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Median change from Baseline in CD4+ cell counts at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and from Week 48 every 12 weeks until study completion

End point title	Median change from Baseline in CD4+ cell counts at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, and from Week 48 every 12 weeks until study completion

End point description:

Median change from Baseline in CD4+ cell counts was assessed at Day 8 and Weeks 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, and 180. Change from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants with data available at the indicated time points were considered for analysis (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT-E Population.

End point type	Secondary

End point timeframe:

Baseline; Day 8; Weeks 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168 and 180.

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[19]			
Units: Cells per millimeters cubed (cells/mm^3)				
median (inter-quartile range (Q1-Q3))				
CD4+, Day 8, n=181	20 (0 to 60)			
CD4+, Week 4, n=178	30 (0 to 71)			
CD4+, Week 8, n=178	40 (0 to 81)			
CD4+, Week 12, n=171	50 (0 to 100)			
CD4+, Week 16, n=165	60 (20 to 130)			
CD4+, Week 24, n=163	61 (20 to 130)			

CD4+, Week 32, n=147	100 (20 to 160)			
CD4+, Week 40, n=143	90 (30 to 180)			
CD4+, Week 48, n=145	110 (40 to 190)			
CD4+, Week 60, n=142	120 (50 to 210)			
CD4+, Week 72, n=138	140 (60 to 231)			
CD4+, Week 84, n=137	150 (80 to 240)			
CD4+, Week 96, n=117	160 (80 to 270)			
CD4+, Week 108, n=98	180.5 (80 to 280)			
CD4+, Week 120, n=82	180 (100 to 280)			
CD4+, Week 132, n=61	221 (100 to 320)			
CD4+, Week 144, n=46	205 (130 to 350)			
CD4+, Week 156, n=32	225 (155 to 345)			
CD4+, Week168, n=24	265 (155 to 380)			
CD4+, Week180, n=6	170.5 (140 to 230)			

Notes:

[19] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio of CD4+/CD8+ cell count at Baseline and Weeks 4, 12, 24, and 48

End point title	Ratio of CD4+/CD8+ cell count at Baseline and Weeks 4, 12, 24, and 48

End point description:

The ratio of CD4+/CD8+ cell count (measured in cells/mm^3) was assessed at Baseline and at Weeks 4, 12, 24, and 48. The ratio was calculated as the CD4+ cell count divided by CD8+ cell count. Only those participants with data available at the indicated time points were considered for analysis (represented by n=X in the category titles). Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the ITT-E Population.

End point type	Secondary

End point timeframe:

Baseline; Weeks 4, 12, 24, and 48

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[20]			
Units: ratio				
median (inter-quartile range (Q1-Q3))				
Baseline, n=180	0.15 (0.05 to 0.34)			

Week 4, n=176	0.19 (0.09 to 0.37)			
Week 12, n=170	0.21 (0.1 to 0.46)			
Week 24, n=154	0.26 (0.14 to 0.46)			
Week 48, n=140	0.32 (0.19 to 0.52)			

Notes:

[20] - ITT-E population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with HIV-1 disease progression (Acquired Immune Deficiency Syndrome [AIDS] or death)

End point title	Number of participants with HIV-1 disease progression (Acquired Immune Deficiency Syndrome [AIDS] or death)

End point description:

The number of participants with HIV-1 disease progression (AIDS or death) was assessed per the Centers for Disease Control and Prevention (CDC) 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. The CDC classifies HIV infection as Category A (participants with asymptomatic HIV infection, acute HIV infection with accompanying illness, or persistent generalized lymphadenopathy), Category B (participants with symptomatic non-AIDS condition, i.e., conditions that are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or conditions are considered by physicians to have a clinical course or to require management that is complicated by HIV infection), and Category C (includes AIDS indicator conditions as defined by diagnostic or presumptive measures).

End point type	Secondary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[21]			
Units: Participants				
number (not applicable)				
Progression from CDC Class A to Class C Event	1			
Progression from CDC Class B to Class C Event	2			
Progression from CDC Class C to New Class C Event	6			
Progression from Classes A, B, or C to Death	2			

Notes:

[21] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax and Ctau of DTG

End point title	Cmax and Ctau of DTG

End point description:

The maximum plasma concentration (Cmax) and the concentration at the end of a dosing interval (Ctau) of DTG were assessed by a population pharmacokinetic (PK) modeling approach using pooled DTG PK data from multiple studies. For this study, blood samples for pharmacokinetic assessments were collected pre-dose on Day 8 and at Weeks 4 and 24, at 1-3 hours post-dose on Day 8, and at 1-3 hours or 4-12 hours post-dose at Weeks 4 and 24. The Pharmacokinetic (PK) Concentration Population used is defined as all subjects who received DTG, had undergone PK sampling during the study, and provided evaluable DTG plasma concentration data.

End point type	Secondary

End point timeframe:

Day 8, Week 4, and Week 24

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[22]			
Units: Micrograms per milliliter (µg/mL)				
geometric mean (confidence interval 95%)				
Cmax	4.74 (4.18 to 5.36)			
Ctau	2.6 (2.15 to 3.15)			

Notes:

[22] - The Pharmacokinetic (PK) Concentration Population

Statistical analyses

No statistical analyses for this end point

Secondary: AUC(0-tau) and AUC(0-24) of DTG

End point title	AUC(0-tau) and AUC(0-24) of DTG

End point description:

The area under the time concentration curve over the dosing interval (AUC[0-tau]) and from 0 to 24 hours (AUC[0-24]) of DTG was assessed by a population PK modeling approach using pooled DTG PK data from multiple studies. For this study, blood samples for pharmacokinetic assessments were collected pre-dose on Day 8 and at Weeks 4 and 24, at 1-3 hours post-dose on Day 8, and at 1-3 hours or 4-12 hours post-dose at Weeks 4 and 24. The Pharmacokinetic (PK) Concentration Population used is defined as all subjects who received DTG, had undergone PK sampling during the study, and provided evaluable DTG plasma concentration data.

End point type	Secondary

End point timeframe:

Day 8, Week 4, and Week 24

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	183[23]			
Units: µg*hour/mL				
geometric mean (confidence interval 95%)				
AUC(0-tau)	36.7 (35 to 38.6)			
AUC(0-24)	73.5 (70 to 77.1)			

Notes:

[23] - The Pharmacokinetic (PK) Concentration Population

Statistical analyses

No statistical analyses for this end point

Secondary: C0 assessment of DTG

End point title	C0 assessment of DTG

End point description:

The plasma DTG concentration immediately prior to dosing at steady state (C0) was assessed at Day 8, Week 4, and Week 24. Blood samples for pharmacokinetic assessments were collected pre-dose and 1-3 hours post-dose on Day 8 and at Week 4 and 4-12 hours post-dose at Week 24. Different participants may have been analyzed at different time points, so the overall number of participants analyzed reflects everyone in the Pharmacokinetic Parameter Population. The Pharmacokinetic (PK) Concentration Population used is defined as all subjects who received DTG, had undergone PK sampling during the study, and provided evaluable DTG plasma concentration data.

End point type	Secondary

End point timeframe:

Day 8, Week 4, and Week 24

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	161[24]			
Units: µg/mL				
geometric mean (geometric coefficient of variation)				
Day 8, n=148	2.36 (± 91)			
Week 4, n=161	1.9 (± 113)			
Week 24, n=135	2.14 (± 93)			

Notes:

[24] - Pharmacokinetic (PK) Parameter Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated treatment-emergent integrase (IN) mutations detected at the time of protocol-defined virologic failure (PDVF) as a measure of genotypic resistance

End point title	Number of participants with the indicated treatment-emergent integrase (IN) mutations detected at the time of protocol-defined virologic failure (PDVF) as a measure of genotypic resistance

End point description:

Analysis of changes at specific amino acids in the IN coding region associated with resistance to raltegravir, elvitegravir, or DTG was performed at Day 1 and at the time of PDVF. PDVF is a <0.5 log10 c/mL decrease in plasma HIV-1 RNA at Day 8 unless the absolute value is <400 c/mL. PDVF after Day 8 is defined as virological non-responses (decrease in plasma HIV-1 RNA of <1 log10 c/mL by Week 16, with subsequent confirmation, unless plasma HIV-1 RNA <400 c/mL and confirmed plasma HIV-1 RNA levels >=400 c/mL on or after Week 24) & virological rebound (confirmed rebound in plasma HIV-1 RNA levels to >=400 c/mL after prior confirmed suppression to <400 c/mL & confirmed plasma HIV-1 RNA levels >1 log10 c/mL above the nadir value [nadir: >=400 c/mL]). PDVF Genotypic Resistance (GR) populations: all par. in the ITT-E Population with available on-treatment GR data at the time of PDVF. Only par. with baseline IN mutations with PDVF who had paired baseline and time of PDVF samples considered.

End point type	Secondary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	42[25]			
Units: participants				
number (not applicable)				
Any IN mutation	25			
T97A	8			
T97T/A	4			
E138A	1			
E138E/A	1			
E138E/K	3			
E138K	4			
E138T/A	1			
N155H	6			
N155N/H	1			
Q148H	3			
Q148Q/H	2			
Q148R	1			
Q148Q/R/K	1			
G140G/S	1			
G140S	3			
L74L/M/V	1			
L74L/M	1			
L74I	1			
E92E/Q	2			
S147G	2			
E157E/Q	1			
V151V/M/I	1			
Y143Y/H	1			

Notes:

[25] - PDVF Genotypic Resistance Populations

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated fold increase in DTG FC (fold change in IC50 [50% inhibitory concentration] relative to wild-type virus) between Baseline and the time of PDVF, as a measure of post-Baseline phenotypic resistance

End point title	Number of participants with the indicated fold increase in DTG FC (fold change in IC50 [50% inhibitory concentration] relative to wild-type virus) between Baseline and the time of PDVF, as a measure of post-Baseline phenotypic resistance

End point description:

The FC in IC50 for DTG relative to wild-type virus was determined for virus isolated at Baseline & at the time of PDVF. The number of participants with the indicated change (ratio) in the two values at the time of PDVF is presented. PDVF is defined as a <0.5 log10 c/mL decrease in plasma HIV-1 RNA at Day 8 unless the absolute value is <400 c/mL. PDVF after Day 8 was defined for virological non-response (decrease in plasma HIV-1 RNA of less than 1 log10 c/mL by Week 16, with subsequent confirmation, unless plasma HIV-1 RNA <400 c/mL and confirmed plasma HIV-1 RNA levels >=400 c/mL on or after Week 24) & virological rebound (confirmed rebound in plasma HIV-1 RNA levels to >=400 c/mL after prior confirmed suppression to <400 c/mL and confirmed plasma HIV-1 RNA levels >1 log10 c/mL above the nadir value, where nadir is >=400 c/mL). PDVF Phenotypic Resistance Populations are the only par. with Baseline DTG IC50 with PDVF who had paired Baseline & time of virological failure are considered.

End point type	Secondary

End point timeframe:

From the day of the first dose of study drug until end of treatment visit for each participant, up to Week 180 (median of 758 days)

End point values	Dolutegravir 50 mg BID			
Subject group type	Reporting group			
Number of subjects analysed	45[26]			
Units: Participants				
number (not applicable)				
<1 fold	6			
1-<2 fold	16			
2-<4 fold	4			
4-<8 fold	4			
>=8 fold	12			
Missing	3			

Notes:

[26] - PDVF Phenotypic Resistance Populations.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On treatment serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of study treament until the end of treatment visit for each participant (up to Week 180)

Adverse event reporting additional description:

On-treatment SAEs and non-serious AEs were reported for the Safety population consisted of all participants who received at least one dose of investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Dolutegravir 50 mg BID

Reporting group description:

Participants received DTG 50 mg BID.

Serious adverse events	Dolutegravir 50 mg BID		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 183 (25.14%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bowen's disease			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	2 / 183 (1.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anogenital warts			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bile duct cancer			

subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hodgkin's disease recurrent				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anal cancer stage I				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
B-cell lymphoma				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hodgkin's disease				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lip and/or oral cavity cancer				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lip and/or oral cavity cancer stage 0				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the cervix				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertensive emergency				

subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 183 (1.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Immune reconstitution inflammatory syndrome			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian mass			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	2 / 183 (1.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Productive cough			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			

subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	2 / 183 (1.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchopneumopathy			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Bipolar disorder			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	2 / 183 (1.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Coronary artery disease			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nerve compression			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Parotid gland enlargement				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 183 (1.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haematochezia				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Aphthous stomatitis				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				

subjects affected / exposed	2 / 183 (1.09%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatic cirrhosis				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis acute				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bile duct obstruction				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Drug-induced liver injury				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatocellular injury				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nodular regenerative hyperplasia				
subjects affected / exposed	1 / 183 (0.55%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Drug eruption				

subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pruritus			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash generalised			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Tendonitis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint destruction			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 183 (2.73%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	2 / 183 (1.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cytomegalovirus infection			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epstein-Barr virus infection			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes ophthalmic			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes zoster			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Lung infection			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal candidiasis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumococcal sepsis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Streptococcal sepsis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye infection toxoplasmal			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes virus infection			

subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatitis B			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oral candidiasis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Orchitis			
subjects affected / exposed	1 / 183 (0.55%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 183 (1.64%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Dolutegravir 50 mg BID		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	143 / 183 (78.14%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	11		
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 183 (13.11%)		
occurrences (all)	27		
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	17 / 183 (9.29%)		
occurrences (all)	17		
Pyrexia			
subjects affected / exposed	19 / 183 (10.38%)		
occurrences (all)	25		
Asthenia			
subjects affected / exposed	13 / 183 (7.10%)		
occurrences (all)	17		
Injection site reaction			
subjects affected / exposed	12 / 183 (6.56%)		
occurrences (all)	12		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	41 / 183 (22.40%)		
occurrences (all)	53		
Nausea			
subjects affected / exposed	26 / 183 (14.21%)		
occurrences (all)	29		
Vomiting			
subjects affected / exposed	13 / 183 (7.10%)		
occurrences (all)	13		
Abdominal pain upper			
subjects affected / exposed	14 / 183 (7.65%)		
occurrences (all)	14		
Constipation			
subjects affected / exposed	12 / 183 (6.56%)		
occurrences (all)	14		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	29 / 183 (15.85%)		
occurrences (all)	36		
Oropharyngeal pain			
subjects affected / exposed	10 / 183 (5.46%)		
occurrences (all)	10		

Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	17 / 183 (9.29%)		
occurrences (all)	19		
Pruritus			
subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	14		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	14 / 183 (7.65%)		
occurrences (all)	15		
Anxiety			
subjects affected / exposed	10 / 183 (5.46%)		
occurrences (all)	11		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	18 / 183 (9.84%)		
occurrences (all)	22		
Arthralgia			
subjects affected / exposed	12 / 183 (6.56%)		
occurrences (all)	17		
Pain in extremity			
subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	13		
Infections and infestations			
Bronchitis			
subjects affected / exposed	25 / 183 (13.66%)		
occurrences (all)	35		
Upper respiratory tract infection			
subjects affected / exposed	22 / 183 (12.02%)		
occurrences (all)	25		
Nasopharyngitis			
subjects affected / exposed	12 / 183 (6.56%)		
occurrences (all)	14		
Rhinitis			

subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	14		
Influenza			
subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	11		
Sinusitis			
subjects affected / exposed	11 / 183 (6.01%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2011	Clarification of statistical algorithm (MSDF), guidance on Entecavir use provided, cautionary text added to Permitted Medications and Non-Drug Therapies section, Rifapentine added to Prohibited Medications plus additional guidance, management of subjects with Decline in Renal Function amended, addition of section on Rash management, addition of ATV use to exceptions statement in Appendix 3: Child-Pugh classification, correction of typographical errors and minor edits.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported