Clinical trial results:
A Phase 3, randomized, double-blind study of the safety and efficacy of GSK1349572 plus abacavir/lamivudine fixed-dose combination therapy administered once daily compared to Atripla over 96 weeks in HIV-1 infected antiretroviral therapy naive adult subjects.

Summary

EudraCT number	2010-020983-39
Trial protocol	NL DE ES GB HU DK BE IT
Global end of trial date	03 December 2015

Results information

Result version number	v1 (current)
This version publication date	13 August 2016
First version publication date	13 August 2016

Trial information

Trial identification

Sponsor protocol code	ING114467

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	24 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the antiviral activity of GSK1349572 plus ABC/3TC FDC once daily therapy compared to Atripla over 48 weeks in HIV-1 infected therapy-naive subjects.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 February 2011
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	27 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Romania: 18
Country: Number of subjects enrolled	Spain: 235
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Germany: 71
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Australia: 18
Country: Number of subjects enrolled	Canada: 59
Country: Number of subjects enrolled	United States: 325
Worldwide total number of subjects	844
EEA total number of subjects	442

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)	837
From 65 to 84 years	6
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Study consisted of 96 weeks double-blind phase, followed by a 48 week open-label phase.

Pre-assignment

Screening details:

A total of 844 participants (par.) were randomized (1:1) to one of the two treatment arms. Of these, 833 par. received at least one dose of study medication. Of the 11 par. who were randomized but not treated with investigational product, 7 par. withdrew consent, 3 par. were randomized in error, and 1 par. was lost to follow-up.

Period 1

Period 1 title	Double-blind phase: 96 weeks duration
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG 50 mg plus ABC/3TC 600/300 mg once daily

Arm description:

During double-blind phase, participants received a dolutegravir (DTG) 50 milligram (mg) tablet along with an Abacavir/Lamivudine (ABC/3TC) 600/300 mg tablet once daily (OD) orally, with placebo to match Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) 600/200/300 mg for 96 weeks.

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:

50 mg tablet once daily for 96 weeks in double-blind randomized phase

Investigational medicinal product name	Abacavir/Lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/300 mg tablet once daily for 96 weeks in double-blind randomized phase

Investigational medicinal product name	Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet once daily for 96 weeks in double-blind randomized phase.

Arm title	EFV/TDF/FTC 600/200/300 mg once daily

Arm description:

During double-blind phase, participants received EFV/TDF/FTC 600/200/300 mg OD, with placebo to

match DTG 50 mg and ABC/3TC 600/300 mg for 96 weeks.

Arm type	Active comparator
Investigational medicinal product name	Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/200/300 mg tablet once daily for 96 weeks in double-blind randomized phase

Investigational medicinal product name	Dolutegravir (DTG) placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet once daily for 96 weeks in double-blind randomized phase

Investigational medicinal product name	Abacavir/Lamivudine (ABC/3TC) Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One tablet once daily for 96 weeks in double-blind randomized phase

Number of subjects in period 1[1]	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily
Started	414	419
Completed	342	310
Not completed	72	109
Adverse event, serious fatal	-	2
Physician decision	1	2
Consent withdrawn by subject	9	15
Adverse event, non-fatal	13	46
Lost to follow-up	17	18
Lack of efficacy	18	14
Protocol deviation	14	12

Notes:

[1] - 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: A total of 844 participants (par.) were randomized (1:1) to one of the two treatment arms. Of these, 833 par. received at least one dose of study medication. Of the 11 par. who were randomized but not treated with investigational product, 7 par. withdrew consent, 3 par. were randomized in error, and 1 par. was lost to follow-up.

Period 2

Period 2 title	Open-label phase: 48 weeks duration
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG 50 mg plus ABC/3TC 600/300 mg once daily

Arm description:

Participants who completed double-blind phase continued to receive DTG 50 mg tablet along with ABC/3TC 600/300 mg tablet OD orally, for additional 48 weeks during open-label phase.

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

Dosage and administration details:

50 mg tablet once daily for 48 weeks in open-label phase (96 weeks through 144 week), and during open-label continuation phase until dolutegravir is commercially approved.

Investigational medicinal product name	Abacavir/Lamivudine (ABC/3TC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/300 mg tablet once daily for 48 weeks in open-label phase (96 weeks through 144 week), and during open-label continuation phase until dolutegravir is commercially approved.

Arm title	EFV/TDF/FTC 600/200/300 mg once daily

Arm description:

Participants who completed double-blind phase continued to receive EFV/TDF/FTC 600/200/300 mg OD for additional 48 weeks during open-label phase.

Arm type	Active comparator
Investigational medicinal product name	Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

600/200/300 mg tablet once daily for 48 weeks in open-label phase (96 weeks through 144 week).

Number of subjects in period 2[2]	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily
Started	341	309
Completed	317	278
Not completed	24	31
Consent withdrawn by subject	3	7

Physician decision	-	2
Adverse event, non-fatal	3	10
Lost to follow-up	8	8
Lack of efficacy	7	2
Protocol deviation	3	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: One subject in each treatment group elected not to enter the Open-label phase; however, they are considered to have completed the study.

Baseline characteristics

Reporting groups	
Reporting group title	DTG 50 mg plus ABC/3TC 600/300 mg once daily
Reporting group description:	
During double-blind phase, participants received a dolutegravir (DTG) 50 milligram (mg) tablet along with an Abacavir/Lamivudine (ABC/3TC) 600/300 mg tablet once daily (OD) orally, with placebo to match Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) 600/200/300 mg for 96 weeks.	
Reporting group title	EFV/TDF/FTC 600/200/300 mg once daily
Reporting group description:	
During double-blind phase, participants received EFV/TDF/FTC 600/200/300 mg OD, with placebo to match DTG 50 mg and ABC/3TC 600/300 mg for 96 weeks.	

Reporting group values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily	Total
Number of subjects	414	419	833
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	36.5	36.4	
standard deviation	± 10.74	± 10.43	-
Gender categorical			
Units: Subjects			
Female	67	63	130
Male	347	356	703
Race			
Units: Subjects			
African American (Af Am)/African Heritage (Af Ht)	98	99	197
American Indian (AI) or Alaska Native (Nat)	13	17	30
Asian	9	9	18
White	284	285	569
Af Am/Af Ht & AI or Alaska Native	0	1	1
Af Am/Af Ht & Nat Hawaiian/other Pacific Islander	0	1	1
Af Am/Af Ht & White	3	2	5
American Indian or Alaska Native & White	6	4	10
Asian & White	1	0	1
Missing	0	1	1

End points

End points reporting groups

Reporting group title	DTG 50 mg plus ABC/3TC 600/300 mg once daily

Reporting group description:

During double-blind phase, participants received a dolutegravir (DTG) 50 milligram (mg) tablet along with an Abacavir/Lamivudine (ABC/3TC) 600/300 mg tablet once daily (OD) orally, with placebo to match Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) 600/200/300 mg for 96 weeks.

Reporting group title	EFV/TDF/FTC 600/200/300 mg once daily

Reporting group description:

During double-blind phase, participants received EFV/TDF/FTC 600/200/300 mg OD, with placebo to match DTG 50 mg and ABC/3TC 600/300 mg for 96 weeks.

Reporting group title	DTG 50 mg plus ABC/3TC 600/300 mg once daily

Reporting group description:

Participants who completed double-blind phase continued to receive DTG 50 mg tablet along with ABC/3TC 600/300 mg tablet OD orally, for additional 48 weeks during open-label phase.

Reporting group title	EFV/TDF/FTC 600/200/300 mg once daily

Reporting group description:

Participants who completed double-blind phase continued to receive EFV/TDF/FTC 600/200/300 mg OD for additional 48 weeks during open-label phase.

Subject analysis set title	DTG 50 mg plus ABC/3TC 600/300 mg once daily
Subject analysis set type	Sub-group analysis

Subject analysis set description:

During double-blind phase, participants received a dolutegravir (DTG) 50 milligram (mg) tablet along with an Abacavir/Lamivudine (ABC/3TC) 600/300 mg tablet once daily (OD) orally, with placebo to match Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) 600/200/300 mg for 96 weeks. Participants who completed double-blind phase continued to receive DTG 50 mg tablet along with ABC/3TC 600/300 mg tablet OD orally, for additional 48 weeks during open-label phase.

Subject analysis set title	EFV/TDF/FTC 600/200/300 mg once daily
Subject analysis set type	Sub-group analysis

Subject analysis set description:

During double-blind phase, participants received EFV/TDF/FTC 600/200/300 mg OD, with placebo to match DTG 50 mg and ABC/3TC 600/300 mg for 96 weeks. Participants who completed double-blind phase continued to receive EFV/TDF/FTC 600/200/300 mg OD for additional 48 weeks during open-label phase.

Primary: Proportion of Subjects Responding based on Plasma HIV-1 RNA <50 c/mL at Week 48

End point title	Proportion of Subjects Responding based on Plasma HIV-1 RNA <50 c/mL at Week 48

End point description:

The percentage of participants with plasma HIV-1 RNA <50 c/mL at Week 48 was assessed. Plasma samples were collected for the quantitative assessment of HIV-1 RNA based on the Missing, Switch, or Discontinuation equals Failure (MSDF) algorithm, as codified by the Food and Drug Administration's Snapshot algorithm. This algorithm treats all participants without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of investigational product prior to the visit window) as non-responders, as well as participants who switched their concomitant antiretroviral therapy (ART) in certain scenarios. Since changes in ART were not permitted in this protocol, all such participants who changed ART were to be considered non-responders. Otherwise, virologic success or failure was to be determined by the last available HIV-1 RNA assessment while the participant was on treatment within the visit of interest window. Intent-to-Treat-Exposed (ITT-E) Population.

End point type	Primary

End point timeframe:

Week 48

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[1]	419[2]		
Units: Percentage of participants				
number (not applicable)	88	81		

Notes:

[1] - ITT-E Population: all randomized par. who received at least one dose of study medication

[2] - ITT-E Population: all randomized par. who received at least one dose of study medication

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The estimated value reflects the percentage on DTG + ABC/3TC minus the percentage on EFV/TDF/FTC.

Comparison groups	DTG 50 mg plus ABC/3TC 600/300 mg once daily v EFV/TDF/FTC 600/200/300 mg once daily
Number of subjects included in analysis	833
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	= 0.003 [4]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Difference in percentage
Point estimate	7.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.3
upper limit	12.2

Notes:

[3] - Non-inferiority could be concluded if the lower bound of a two-sided 95% confidence interval for the difference (DTG + ABC/3TC minus EFV/TDF/FTC) in percentages between the two treatment arms was > -10%.

[4] - P-value is for the test of superiority.

Secondary: Time to viral suppression (<50 c/mL)

End point title	Time to viral suppression (<50 c/mL)

End point description:

Viral suppression is defined as the first viral load value<50 c/mL. The Kaplan-Meier method was used to estimate time to viral suppression, defined as the time from the first dose of study treatment until the first viral load value <50 c/mL was reached. Participants who withdrew for any reason without having suppressed prior to the analysis were censored.

End point type	Secondary

End point timeframe:

From Baseline until Week 144) (average of 877.4 days for DTG; average of 788.8 study days for EFV/TDF/FTC)

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[5]	419[6]		
Units: Days				
median (confidence interval 95%)	28 (28 to 29)	84 (83 to 84)		

Notes:

[5] - ITT-E Population

[6] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma human immunodeficiency virus - 1 (HIV-1) ribonucleic acid (RNA) <50 copies/milliliter (c/mL) at Week 96 and Week 144

End point title	Percentage of participants with plasma human immunodeficiency virus -1 (HIV-1) ribonucleic acid (RNA) <50 copies/milliliter (c/mL) at Week 96 and Week 144

End point description:

The percentage of participants with plasma HIV-1 RNA <50 c/mL at Week 96 and Week 144 was assessed. Plasma samples were collected for the quantitative assessment of HIV-1 RNA based on the Missing, Switch, or Discontinuation equals Failure (MSDF) algorithm, as codified by the Food and Drug Administration's Snapshot algorithm. This algorithm treats all participants without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of investigational product prior to the visit window) as non-responders, as well as participants who switched their concomitant antiretroviral therapy (ART) in certain scenarios. Since changes in ART were not permitted in this protocol, all such participants who changed ART were to be considered non-responders. Otherwise, virologic success or failure was to be determined by the last available HIV-1 RNA assessment while the participant was on treatment within the visit of interest window.

End point type	Secondary

End point timeframe:

Week 96 and Week 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[7]	419[8]		
Units: Percentage of participants				
number (not applicable)				
Week 96	77	70		
Week 144	71	63		

Notes:

[7] - ITT-E Population

[8] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 96:The estimated value reflects the percentage on DTG + ABC/3TC minus the percentage on EFV/TDF/FTC.

Comparison groups	DTG 50 mg plus ABC/3TC 600/300 mg once daily v EFV/TDF/FTC 600/200/300 mg once daily
Number of subjects included in analysis	833
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	= 0.016 [10]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Difference in percentage
Point estimate	7.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	13.1

Notes:

[9] - Non-inferiority could be concluded if the lower bound of a two-sided 95% confidence interval for the difference (DTG + ABC/3TC minus EFV/TDF/FTC) in percentages between the two treatment arms was > -10%.
[10] - P-value is for the test of superiority.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 144:Estimated value reflects the percentage on DTG + ABC/3TC minus the percentage on EFV/TDF/FTC.

Comparison groups	DTG 50 mg plus ABC/3TC 600/300 mg once daily v EFV/TDF/FTC 600/200/300 mg once daily
Number of subjects included in analysis	833
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
P-value	= 0.01 [12]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Difference in percentage
Point estimate	8.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.9
upper limit	14.6

Notes:

[11] - Non-inferiority could be concluded if the lower bound of a two-sided 95% confidence interval for the difference (DTG + ABC/3TC minus EFV/TDF/FTC) in percentages between the two treatment arms was >-10%.
[12] - P-value is for the test of superiority.

Secondary: Number of participants with a confirmed plasma HIV-1 RNA level >=1000 c/mL at or after Week 16 and before Week 24, or a confirmed plasma HIV-1 RNA level >=200 c/mL at or after Week 24

End point title	Number of participants with a confirmed plasma HIV-1 RNA level >=1000 c/mL at or after Week 16 and before Week 24, or a confirmed plasma HIV-1 RNA level >=200 c/mL at or after Week 24

End point description:

Data are presented as Kaplan Meier estimates of virologic failure (VF), defined as a confirmed plasma HIV-1 RNA level >=1000 c/mL at or after Week 16 and before Week 24, or a confirmed plasma HIV-1 RNA level >=200 c/mL at or after Week 24. A plasma HIV-1 RNA value was considered to be confirmed failure if a consecutive measurement satisfied the same failure criterion. The number of participants who experienced autoimmune deficiency syndrome (AIDS) Clinical Trials Group (ACTG) VFs was measured. For participants who withdrew from the study/were not documented to have reached confirmed VF at the cut off date of the Week 48 analysis, time to VF was to be censored at the planned visit week of the last measured plasma HIV-1 RNA sample. Data for participants who missed three consecutive scheduled plasma HIV-1 RNA measurements were to be censored at the planned visit week of the last assessment prior to the 3 consecutive missed visits.

End point type	Secondary

End point timeframe:

From Baseline until Week 144) (average of 877.4 days for DTG; average of 788.8 study days for EFV/TDF/FTC)

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[13]	419[14]		
Units: Participants				
number (not applicable)				
ACTG virologic failures	11	8		
Censored participants	403	411		

Notes:

[13] - ITT-E Population

[14] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in plasma HIV-1 RNA at Weeks 2, 4, 8, 12, 16, 24, 32, 40,48, 60, 72, 84, 96, 108, 120, 132 and 144

End point title	Change from Baseline in plasma HIV-1 RNA at Weeks 2, 4, 8, 12, 16, 24, 32, 40,48, 60, 72, 84, 96, 108, 120, 132 and 144

End point description:

Blood samples were collected for the measurement of HIV-1 RNA in plasma. Changes from Baseline was calculated as the post-Baseline value minus the Baseline value. Only those participants available at the indicated time points were assessed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 2, 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132 and 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[15]	419[16]		
Units: log10 copies/mL				
arithmetic mean (standard deviation)				
Week 2, n=387, 376	-2.46 (± 0.49)	-1.96 (± 0.46)		
Week 4, n=404, 391	-2.88 (± 0.58)	-2.25 (± 0.52)		
Week 8, n=395, 386	-2.99 (± 0.64)	-2.6 (± 0.6)		
Week 12, n=394, 377	-3.01 (± 0.7)	-2.85 (± 0.63)		
Week 16, n=386, 366	-3.03 (± 0.66)	-2.98 (± 0.65)		
Week 24, n=389, 364	-3.05 (± 0.69)	-3.01 (± 0.76)		
Week 32, n=380, 355	-3.04 (± 0.7)	-3.05 (± 0.72)		
Week 40, n=370, 345	-3.05 (± 0.68)	-3.04 (± 0.7)		
Week 48, n=370, 343	-3.03 (± 0.69)	-3.04 (± 0.69)		
Week 60, n=360, 330	-3.03 (± 0.67)	-3.05 (± 0.69)		
Week 72, n=354, 320	-3.03 (± 0.7)	-3.06 (± 0.7)		
Week 84, n=353, 314	-3.02 (± 0.7)	-3.07 (± 0.68)		
Week 96, n=345, 310	-2.99 (± 0.73)	-3.06 (± 0.68)		
Week 108, n=340, 300	-3.01 (± 0.71)	-3.08 (± 0.67)		
Week 120, n=333, 289	-3 (± 0.77)	-3.07 (± 0.67)		
Week 132, n=323, 284	-3.03 (± 0.68)	-3.06 (± 0.67)		
Week 144, n=313,269	-3.02 (± 0.72)	-3.04 (± 0.69)		

Notes:

[15] - ITT-E Population

[16] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ cell counts at Week 144

End point title	Change from Baseline in CD4+ cell counts at Week 144

End point description:

Cluster of differentiation (CD4) lymphocyte cells (also called T-cells or T-helper cells) are the primary targets of HIV. The CD4 count and the CD4 percentage mark the degree of immunocompromise. The CD4 count is used to stage the patient's disease, determine the risk of opportunistic illnesses, assess prognosis, and guide decisions about when to start antiretroviral therapy. Change from Baseline was calculated as the Week 144 value minus the Baseline value. The least squares mean is the estimated mean change from Baseline in CD4+ cell counts at Week 144 calculated from a repeated measures model including the following covariates: treatment, visit, Baseline plasma HIV-1 RNA, Baseline CD4+ cell count, treatment*visit interaction, Baseline HIV-1 RNA*visit interaction, and Baseline CD4+ cell count*visit interaction. No assumptions were made about the correlations between a participant's readings of CD4+, i.e., the correlation matrix for within-participant errors is unstructured.

End point type	Secondary

End point timeframe:

Baseline and Week 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[17]	419[18]		
Units: cells per millimeters cubed (cells/mm^3)				
least squares mean (standard error)	378.48 (± 10.99)	331.57 (± 11.59)		

Notes:

[17] - ITT-E Population

[18] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	DTG 50 mg plus ABC/3TC 600/300 mg once daily v EFV/TDF/FTC 600/200/300 mg once daily
Number of subjects included in analysis	833
Analysis specification	Pre-specified
Analysis type	non-inferiority[19]
P-value	= 0.003 [20]
Method	Repeated Measure Mixed Model

Notes:

[19] - Adjusted mean is the estimated mean change from baseline (BL) in CD4 + Cell Count at Week 144 in each arm calculated from a repeated measures model including the following covariates: treatment, visit, BL plasma HIV-1 RNA, BL CD4 cell count, treatment*visit interaction, BL HIV-1 RNA*visit interaction and BL CD4 cell count*visit interaction. No assumptions were made about the correlations between a par.’s readings of CD4 i.e. the correlation matrix for within-subject errors is unstructured.

[20] - P-value is for the test of superiority.

Secondary: Change from Baseline in CD4+ cell counts at Weeks 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132 and 144

End point title	Change from Baseline in CD4+ cell counts at Weeks 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132 and 144

End point description:

CD4 lymphocyte cells (also called T-cells or T-helper cells) are the primary targets of HIV. The CD4 count and the CD4 percentage mark the degree of immunocompromise. The CD4 count is used to stage the patient's disease, determine the risk of opportunistic illnesses, assess prognosis, and guide decisions about when to start antiretroviral therapy. Change from Baseline was calculated as the value at Indicated visit minus the Baseline value. Only those participants available at the indicated time points were assessed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and Week 4, 8, 12, 16, 24, 32, 40, 48, 60, 72, 84, 96, 108, 120, 132 and 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[21]	419[22]		
Units: cells per millimeters cubed (cells/mm^3)				

arithmetic mean (standard deviation)				
Week 4, n=404,390	117.6 (± 114.51)	80.9 (± 112.43)		
Week 8, n=396,382	164.6 (± 129.98)	124.4 (± 124.5)		
Week 12, n=394,378	187.5 (± 157.46)	153 (± 131.91)		
Week 16, n=386,366	214.7 (± 173.35)	174.1 (± 132.02)		
Week 24, n=388,361	216.9 (± 162.89)	177.8 (± 147.72)		
Week 32, n=380,353	250.5 (± 172.06)	208.1 (± 152.13)		
Week 40, n=364,347	265.5 (± 187.81)	216.2 (± 158.49)		
Week 48, n=368,344	267.5 (± 192.3)	209.5 (± 164.37)		
Week 60, n=359,330	271.3 (± 188.05)	235.3 (± 171.98)		
Week 72, n=354,319	306.1 (± 202.02)	269.6 (± 180.04)		
Week 84, n=352,314	315.2 (± 197.92)	272.1 (± 172.28)		
Week 96, n=343,309	322.6 (± 205.35)	286 (± 195.7)		
Week 108, n=339,300	349.3 (± 218.76)	298.9 (± 188.41)		
Week 120, n=332,287	347 (± 234.96)	311 (± 198.79)		
Week 132, n=323,283	377.9 (± 205.78)	327.2 (± 175.31)		
Week 144, n=313,270	379.5 (± 221.17)	333.3 (± 189.25)		

Notes:

[21] - ITT-E Population

[22] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated post-baseline HIV-associated conditions and progression, excluding recurrences at Week 144

End point title	Number of participants with the indicated post-baseline HIV-associated conditions and progression, excluding recurrences at Week 144

End point description:

Clinical disease progression (CDP) was assessed according to the Centers for Disease Control and Prevention (CDC) HIV-1 classification system. Category (CAT) A: one or more of the following conditions (CON), without any CON listed in Categories B and C: asymptomatic HIV infection, persistent generalized lymphadenopathy, acute (primary) HIV infection with accompanying illness or history of acute HIV infection. CAT B: symptomatic CON that are attributed to HIV infection or are indicative of a defect in cell-mediated immunity; or that are considered by physicians to have a clinical course or to require management that is complicated by HIV infection; and not included among CON listed in clinical CAT C. CAT C: the clinical CON listed in the AIDS surveillance case definition. Indicators of CDP were defined as: CDC CAT A at Baseline (BS) to a CDC CAT C event (EV); CDC CAT B at BS to a CDC CAT C EV; CDC CAT C at BS to a new CDC CAT C EV; or CDC CAT A, B, or C at BS to death.

End point type	Secondary

End point timeframe:

From Baseline until Week 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[23]	419[24]		
Units: Participants				
number (not applicable)				
Week 144, Any category condition	17	24		
Week 144, Any Category B condition	12	17		
Week 144, Any Category C condition	5	6		
Week 144, Any death	0	2		
Week 144, Progression from CAT A to CAT C	4	4		
Week 144, Progression from CAT C to new CAT C	1	2		
Week 144, Progression from CAT A, B, or C to death	0	2		

Notes:

[23] - ITT-E Population

[24] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated Grade 1 to 4 clinical and hematology toxicities at Week 144

End point title	Number of participants with the indicated Grade 1 to 4 clinical and hematology toxicities at Week 144

End point description:

All Grade 1 to 4 post-Baseline-emergent chemistry toxicities included alanine aminotransferase (ALT), albumin, alkaline phosphatase (ALP), asparate aminotransferase (AST), carbon dioxide (CO2) content/bicarbonate, cholesterol, creatine kinase (CK), creatinine, hyperglycemia, hyperkalemia, hypernatremia, hypoglycemia, hypokalemia, hyponatremia, low density lipoprotein (LDL) cholesterol calculation, lipase, phosphorus inorganic, total bilirubin, and triglycerides. All Grade 1 to 4 post-Baseline-emergent hematology toxicities included hemoglobin, platelet count, total neutrophils, and white blood cell count. The Division of AIDS (DAIDS) defined toxicity grades as follows: Grade 1, mild; Grade 2, moderate; Grade 3, severe; Grade 4, potentially life threatening; Grade 5, death.

End point type	Secondary

End point timeframe:

From Baseline until Week 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	414[25]	419[26]		
Units: Participants				

number (not applicable)				
Week 144, ALT	62	81		
Week 144, Albumin	0	1		
Week 144, ALP	17	53		
Week 144, AST	77	85		
Week 144, CO2 content/bicarbonate	135	134		
Week 144, Cholesterol	156	140		
Week 144, CK	91	79		
Week 144, Creatinine	17	6		
Week 144, Hyperglycaemia	121	105		
Week 144, Hyperkalemia	4	12		
Week 144, Hypernatremia	11	9		
Week 144, Hypoglycaemia	24	21		
Week 144, Hypokalemia	38	21		
Week 144, Hyponatremia	63	86		
Week 144, LDL cholesterol calculation	124	111		
Week 144, Lipase	111	110		
Week 144, Phosphorus, inorganic	109	134		
Week 144, Total bilirubin	22	4		
Week 144, Triglycerides	11	11		
Week 144, Hemoglobin	7	11		
Week 144, Platelet count	20	19		
Week 144, Total neutrophils	70	80		
Week 144, White Blood Cell count	9	18		

Notes:

[25] - Safety Population: all participants who received at least one dose of investigational product

[26] - Safety Population: all participants who received at least one dose of investigational product

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated genotypic resistance with virological failure (VF) through Week 144

End point title	Number of participants with the indicated genotypic resistance with virological failure (VF) through Week 144

End point description:

Whole blood samples were collected from participants to provide plasma for storage samples for potential viral genotypic and phenotypic analyses. Participants with confirmed virological failure (confirmed HIV-1 RNA >=50 copies/mL throughout the study and/or confirmed HIV-1 RNA >=200 copies/mL at Week 144) had plasma samples tested for HIV-1 RT genotype and HIV-1 integrase genotype from Baseline samples and from samples collected at the time of virological failure. Genotype testing was conducted at Day 1 and at the time of suspected protocol-defined virological failure (PDVF). A genotyping assessment was made of change across all amino acids within the integrase (IN)-encoding region, with particular attention paid to specific amino acid changes associated with the development of resistance to RAL, ELV, or DTG. PDVF Genotypic Population: all participants in the ITT-E Population with available on-treatment genotypic resistance data at the time of PDVF.

End point type	Secondary

End point timeframe:

Through Week 144

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26[27]	16[28]		
Units: Participants				
number (not applicable)				
Week 144, RT mutation K65K/R	0	1		
Week 144, RT mutation K101E	0	1		
Week 144, RT mutation K103K/N	0	2		
Week 144, RT mutation K103N	0	2		
Week 144, RT mutation G190G/A	0	2		

Notes:

[27] - PDVF Genotypic Population

[28] - PDVF Genotypic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in the Symptom Bother Score (SBS) at Week 4 through Week 48

End point title	Change from Baseline in the Symptom Bother Score (SBS) at Week 4 through Week 48

End point description:

The Symptom Distress Module (SDM) is a 20-item, self-reported questionnaire measuring the presence/perceived distress linked to symptoms associated with HIV/its treatments. Developed with support from the AIDS Clinical Trials Group of the U.S. National Institute of Allergy and Infectious Diseases, it has demonstrated construct validity and has shown strong associations with physical/mental health summary scores and with disease severity. The SDM consists of 2 main scores: symptom count and the SBS, ranging from 0 (best) to 80 (worst) and based on the degree of bother that each symptom present posed. The SBS was calculated by adding the 20 individual bother item scores, which were calculated as: 0, “I do not have this symptom”; 1, "It doesn’t bother me”; 2, “It bothers me a little”; 3, “It bothers me”; 4, "It bothers me a lot." Estimates are calculated from an analysis of covariance (ANCOVA) model adjusting for age, sex, race, Baseline (BL) viral load, BL CD4+ cell count, and BL SBS.

End point type	Secondary

End point timeframe:

Baseline and Week 4 through 48
Par. with missing bother item scores at Week 4 had their last observation carried forward (LOCF). Only those par. contributing to the model (i.e., without missing response variables after LOCF or covariates) were analyzed.

End point values	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	394[29]	393[30]		
Units: Scores on a scale				
least squares mean (standard error)	-1.818 (± 0.3849)	-1.246 (± 0.3854)		

Notes:
[29] - ITT-E Population
[30] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and non-serious AEs were collected from the start of study medication to Week 144 (average of 877.4 study days for DTG; average of 788.8 study days for EFV/TDF/FTC).

Adverse event reporting additional description:

SAEs and non-serious AEs were collected in members of the Safety Population, comprised of all participants who received at least one dose of investigational product.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	DTG 50 mg plus ABC/3TC 600/300 mg once daily

Reporting group description:

During double-blind phase, participants received a dolutegravir (DTG) 50 milligram (mg) tablet along with an Abacavir/Lamivudine (ABC/3TC) 600/300 mg tablet once daily (OD) orally, with placebo to match Efavirenz/Tenofovir disoproxil fumarate/Emtricitabine (EFV/TDF/FTC) 600/200/300 mg for 96 weeks. Participants who completed double-blind phase continued to receive DTG 50 mg tablet along with ABC/3TC 600/300 mg tablet OD orally, for additional 48 weeks during open-label phase.

Reporting group title	EFV/TDF/FTC 600/200/300 mg once daily

Reporting group description:

During double-blind phase, participants received EFV/TDF/FTC 600/200/300 mg OD, with placebo to match DTG 50 mg and ABC/3TC 600/300 mg for 96 weeks. Participants who completed double-blind phase continued to receive EFV/TDF/FTC 600/200/300 mg OD for additional 48 weeks during open-label phase.

Serious adverse events	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily	
Total subjects affected by serious adverse events			
subjects affected / exposed	65 / 414 (15.70%)	60 / 419 (14.32%)	
number of deaths (all causes)	0	5	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian cancer			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancoast's tumour			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleomorphic adenoma			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 414 (0.24%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ectopic pregnancy			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adverse drug reaction			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			

subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Priapism			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory distress			
subjects affected / exposed	0 / 414 (0.00%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pleural effusion			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pneumothorax spontaneous			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar disorder			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	3 / 414 (0.72%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 414 (0.24%)	3 / 419 (0.72%)	
occurrences causally related to treatment / all	0 / 1	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	2 / 414 (0.48%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Homicidal ideation			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar I disorder			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervousness			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paranoia			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality disorder			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia, paranoid type			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shared psychotic disorder			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal behaviour			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Foot fracture			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	2 / 414 (0.48%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			

subjects affected / exposed	0 / 414 (0.00%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acetabulum fracture			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chemical burn of skin			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
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 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina unstable			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Syncope			
subjects affected / exposed	0 / 414 (0.00%)	3 / 419 (0.72%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 414 (0.00%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coma			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Grand mal convulsion			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasogenic cerebral oedema			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Anaemia			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Febrile neutropenia			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pancreatitis acute			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Renal failure acute			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Renal failure chronic			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Rotator cuff syndrome			
subjects affected / exposed	0 / 414 (0.00%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tendon disorder			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Appendicitis			
subjects affected / exposed	4 / 414 (0.97%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 414 (0.24%)	3 / 419 (0.72%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 414 (0.48%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 414 (0.24%)	2 / 419 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 414 (0.00%)	3 / 419 (0.72%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 414 (0.24%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syphilis			
subjects affected / exposed	2 / 414 (0.48%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
AIDS dementia complex			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis pharyngeal			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Empyema			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Human herpesvirus 6 infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected dermal cyst			

subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis cryptococcal			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycobacterium avium complex infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcal sepsis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scrotal abscess			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			

subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal abscess			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic candida			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxoplasmosis			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 414 (0.00%)	1 / 419 (0.24%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection staphylococcal			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (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			
Diabetes mellitus			

subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 414 (0.24%)	0 / 419 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DTG 50 mg plus ABC/3TC 600/300 mg once daily	EFV/TDF/FTC 600/200/300 mg once daily	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	332 / 414 (80.19%)	358 / 419 (85.44%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	23 / 414 (5.56%)	17 / 419 (4.06%)	
occurrences (all)	25	17	
Nervous system disorders			
Dizziness			
subjects affected / exposed	43 / 414 (10.39%)	154 / 419 (36.75%)	
occurrences (all)	49	177	
Headache			
subjects affected / exposed	67 / 414 (16.18%)	64 / 419 (15.27%)	
occurrences (all)	82	81	
Somnolence			
subjects affected / exposed	10 / 414 (2.42%)	24 / 419 (5.73%)	
occurrences (all)	12	25	
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	67 / 414 (16.18%)	56 / 419 (13.37%)	
occurrences (all)	77	64	
Pyrexia			
subjects affected / exposed	27 / 414 (6.52%)	30 / 419 (7.16%)	
occurrences (all)	32	31	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	94 / 414 (22.71%)	89 / 419 (21.24%)	
occurrences (all)	125	109	
Nausea			
subjects affected / exposed	70 / 414 (16.91%)	63 / 419 (15.04%)	
occurrences (all)	82	68	
Vomiting			
subjects affected / exposed	28 / 414 (6.76%)	27 / 419 (6.44%)	
occurrences (all)	34	36	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	39 / 414 (9.42%)	40 / 419 (9.55%)	
occurrences (all)	43	44	
Oropharyngeal pain			
subjects affected / exposed	32 / 414 (7.73%)	19 / 419 (4.53%)	
occurrences (all)	39	21	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	22 / 414 (5.31%)	63 / 419 (15.04%)	
occurrences (all)	24	71	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	74 / 414 (17.87%)	52 / 419 (12.41%)	
occurrences (all)	89	57	
Abnormal dreams			
subjects affected / exposed	32 / 414 (7.73%)	74 / 419 (17.66%)	
occurrences (all)	34	81	
Depression			
subjects affected / exposed	34 / 414 (8.21%)	38 / 419 (9.07%)	
occurrences (all)	39	40	

Anxiety			
subjects affected / exposed	33 / 414 (7.97%)	35 / 419 (8.35%)	
occurrences (all)	38	42	
Nightmare			
subjects affected / exposed	11 / 414 (2.66%)	21 / 419 (5.01%)	
occurrences (all)	12	26	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	37 / 414 (8.94%)	25 / 419 (5.97%)	
occurrences (all)	44	27	
Arthralgia			
subjects affected / exposed	28 / 414 (6.76%)	24 / 419 (5.73%)	
occurrences (all)	36	31	
Pain in extremity			
subjects affected / exposed	23 / 414 (5.56%)	14 / 419 (3.34%)	
occurrences (all)	25	14	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	86 / 414 (20.77%)	81 / 419 (19.33%)	
occurrences (all)	137	124	
Upper respiratory tract infection			
subjects affected / exposed	69 / 414 (16.67%)	58 / 419 (13.84%)	
occurrences (all)	95	84	
Bronchitis			
subjects affected / exposed	33 / 414 (7.97%)	33 / 419 (7.88%)	
occurrences (all)	39	37	
Syphilis			
subjects affected / exposed	26 / 414 (6.28%)	31 / 419 (7.40%)	
occurrences (all)	28	33	
Sinusitis			
subjects affected / exposed	29 / 414 (7.00%)	18 / 419 (4.30%)	
occurrences (all)	35	21	
Influenza			
subjects affected / exposed	31 / 414 (7.49%)	14 / 419 (3.34%)	
occurrences (all)	35	15	
Gastroenteritis			

subjects affected / exposed occurrences (all)	26 / 414 (6.28%) 28	18 / 419 (4.30%) 22	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 October 2010	Country Specific Amendment for the United Kingdom
14 January 2011	This amendment includes the addition of standard hematology and clinical chemistry laboratory assessments as being required for all subjects at the Week 2 study visit. Minor clarifications and corrections have been incorporated.
10 October 2011	This amendment allows for a change in the management of subjects with protocol-defined virologic failure. Additional follow-up assessments were added to the Liver Chemistry Stopping criteria panel. Planned exploratory bone biomarkers results will not be reported to investigators with one exception.
01 August 2012	This amendment adds an Open-label Randomized Phase to both treatment arms from Week 96 to Week 144 to collect long term efficacy and safety data.
17 August 2012	This amendment enables the use of both the commercial presentation of Atripla and the overcoated Atripla in the Open-label Randomized Phase from Week 96 to Week 144.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported