Clinical trial results:
A Phase III, randomised, double-blind, multicentre, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of dolutegravir plus lamivudine compared to dolutegravir plus tenofovir/emtricitabine in HIV-1-infected treatment-naïve adults

Summary

EudraCT number	2015-004418-95
Trial protocol	DE ES BE NL PT FR IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	11 April 2019
First version publication date	11 April 2019

Trial information

Trial identification

Sponsor protocol code	204861

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, ViiV Healthcare, 1 8664357343,
Scientific contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	09 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2018
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate non-inferior antiviral activity of DTG + 3TC versus DTG + TDF/FTC at 48 weeks in HIV-1-infected, ART-naïve subjects

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 July 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Ethical reason
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 105
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 22
Country: Number of subjects enrolled	Canada: 33
Country: Number of subjects enrolled	France: 27
Country: Number of subjects enrolled	Germany: 19
Country: Number of subjects enrolled	Italy: 78
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Mexico: 60
Country: Number of subjects enrolled	Netherlands: 4
Country: Number of subjects enrolled	Portugal: 16
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 75
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 68
Country: Number of subjects enrolled	Taiwan: 62
Country: Number of subjects enrolled	United States: 113
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	719
EEA total number of subjects	251

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)	715
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study is a randomized, double-blind, parallel-group, non-inferiority study. A total of 87 investigational centers in 18 countries randomized one or more participants. The results are presented based on primary analysis at Week 48. Analysis presented used a data cut-off date of 22-May-2018 (for Week 48 database freeze).

Pre-assignment

Screening details:

Total of 719 participants were enrolled and randomized, however only 714 were dosed in the study and 5 were not dosed due to physician decision (3), protocol deviation (1) and participant's own decision (1).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG + 3TC

Arm description:

Participants received a two-drug regimen of dolutegravir plus lamivudine (DTG + 3TC) once daily for 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir (DTG)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet, Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive DTG 50 mg tablet, oral administration, once daily.

Investigational medicinal product name	Lamivudine (3TC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive 3TC 300 mg capsule, oral administration, once daily.

Arm title	DTG + TDF/FTC

Arm description:

Participants received a three-drug regimen of dolutegravir plus tenofovir/emtricitabine (DTG + TDF/FTC) fixed dose combination (FDC) once daily for 48 weeks.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir disoproxil fumarate/emtricitabine fixed-dose combination (TDF/FTC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were randomized to receive 300 mg TDF/ 200 mg FTC capsule, oral administration, once daily.

Number of subjects in period 1[1]	DTG + 3TC	DTG + TDF/FTC
Started	356	358
Completed	0	0
Not completed	356	358
Physician decision	6	3
Consent withdrawn by subject	6	4
Ongoing at Week 48 primary analysis.	320	330
Adverse event, non-fatal	6	4
Protocol Withdrawal Criterion Met	1	6
Lost to follow-up	9	6
Lack of efficacy	3	1
Protocol deviation	5	4

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: Total of 719 participants were enrolled and randomized, however only 714 were dosed in the study and 5 were not dosed due to physician decision (3), protocol deviation (1) and participant's own decision (1).

Baseline characteristics

Reporting groups	
Reporting group title	DTG + 3TC
Reporting group description:	
Participants received a two-drug regimen of dolutegravir plus lamivudine (DTG + 3TC) once daily for 48 weeks.	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of dolutegravir plus tenofovir/emtricitabine (DTG + TDF/FTC) fixed dose combination (FDC) once daily for 48 weeks.	

Reporting group values	DTG + 3TC	DTG + TDF/FTC	Total
Number of subjects	356	358	714
Age categorical Units: Subjects			
Total subjects	356	358	714
Age Continuous Units: Years			
arithmetic mean	34.0	35.0	
standard deviation	± 9.88	± 10.72	-
Sex: Female, Male Units: Subjects			
Female	59	52	111
Male	297	306	603
Race/Ethnicity, Customized Units: Subjects			
American (Am) Indian or Alaska (Al.) native	28	28	56
Asian-Central/South Asian heritage (H.)	0	4	4
Asian - East Asian H.	33	36	69
Asian - South East Asian H.	4	2	6
Black or African Am	44	36	80
Native Hawaiian or other Pacific Islander	2	0	2
White (Wt)-Arabic/North African H.	5	6	11
Wt-Wt/Caucasian (Ca.)/European (Eu.) H.	238	242	480
Black or African Am and Am Indian or Al. native	0	1	1
Black or African Am and Wt-Wt/Ca./Eu. H.	1	1	2
Am Indian or Al. native and Wt-Wt/Ca./Eu. H.	1	2	3

End points

End points reporting groups

Reporting group title	DTG + 3TC
Reporting group description:	
Participants received a two-drug regimen of dolutegravir plus lamivudine (DTG + 3TC) once daily for 48 weeks.	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of dolutegravir plus tenofovir/emtricitabine (DTG + TDF/FTC) fixed dose combination (FDC) once daily for 48 weeks.	

Primary: Percentage of participants with plasma Human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) <50 copies/mL (c/mL) at Week 48

End point title	Percentage of participants with plasma Human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) <50 copies/mL (c/mL) at Week 48
End point description:	
Percentage of participants with HIV-1 RNA<50 c/mL was obtained using Food and Drug Administration (FDA) Snapshot algorithm. The Snapshot algorithm treated 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 switch their concomitant antiretroviral therapy (ART) prior to the visit of interest. This endpoint was analyzed using a stratified analysis with Cochran-Mantel-Haenszel (CMH) weights. Intent-To-Treat Exposed (ITT-E) Population was used which comprised of all randomized participants who receive at least one dose of study treatment.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[1]	358[2]		
Units: Percentage of participants				
number (confidence interval 95%)	90 (86.8 to 93.0)	93 (90.0 to 95.4)		

Notes:

[1] - ITT-E Population

[2] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Difference in proportion was based on CMH stratified analysis adjusting for Baseline stratification factors: Plasma HIV-1 RNA (<=versus [vs.] >100,000 c/mL) and cluster of differentiation 4+ (CD4+) cell count (<= vs. >200 cells per cubic millimeter).	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Adjusted difference in proportion
Point estimate	-2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	1.5

Notes:

[3] - Treatment with DTG+ 3TC was to be declared non-inferior to treatment with DTG+TDF/FTC if the lower end of a two-sided 95% confidence interval for the difference between the two groups in response rates at Week 48 greater than -10%.

Secondary: Percentage of participants with plasma HIV-1 RNA <50 c/mL at Week 24

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL at Week 24

End point description:

Percentage of participants with HIV-1 RNA<50 c/mL was obtained using FDA Snapshot algorithm. The Snapshot algorithm treated 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 switch their concomitant ART prior to the visit of interest. This endpoint was analyzed using a stratified analysis with Cochran-Mantel-Haenszel weights.

End point type	Secondary

End point timeframe:

Week 24

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[4]	358[5]		
Units: Percentage of participants				
number (confidence interval 95%)	92 (89.7 to 95.2)	93 (90.4 to 95.7)		

Notes:

[4] - ITT-E Population

[5] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Difference in proportion was based on CMH stratified analysis adjusting for Baseline stratification factors: Plasma HIV-1 RNA (<=vs.>100,000 c/mL) and CD4+ cell count (<= vs. >200 cells per cubic millimeter).

Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted difference in proportion
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.2
upper limit	3.4

Secondary: Time to viral suppression (HIV-1 RNA <50 c/mL)

End point title	Time to viral suppression (HIV-1 RNA <50 c/mL)

End point description:

Time of viral suppression is defined as the first viral load value <50 c/mL. Nonparametric Kaplan-Meier method was performed. Participants who withdrew for any reason without being suppressed were censored at date of withdrawal. Participants who have not been withdrawn and have not had viral suppression at time of the analysis were censored at last viral load date. Confidence Interval (CI) was estimated using the Brookmeyer-Crowley method. Median along with interquartile range (first Quartile and third Quartile) have been presented.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[6]	358[7]		
Units: Days				
median (inter-quartile range (Q1-Q3))	29.0 (29.0 to 52.0)	29.0 (29.0 to 56.0)		

Notes:

[6] - ITT-E Population

[7] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Hazard ratios were estimated using the Cox proportional hazard regression model. A hazard ratio of >1 indicates that DTG + 3TC is more likely to reach viral suppression earlier than DTG + TDF/FTC.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.558 [8]
Method	Generalized Wilcoxon procedure
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.17

Notes:

[8] - The generalized Wilcoxon procedure was used to estimate a p-value for detecting a difference in cumulative incidence curves between treatment groups.

Secondary: CD4+ cell counts at Weeks 24 and 48

End point title	CD4+ cell counts at Weeks 24 and 48

End point description:

CD4+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Blood samples were collected at specified time points to assess CD4+. It was evaluated by flow cytometry. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Weeks 24 and 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[9]	358[10]		
Units: Cells per cubic millimeter (cells/mm^3)				
arithmetic mean (standard deviation)				
Week 24, n=340,341	655.3 (± 288.32)	632.8 (± 262.61)		
Week 48, n=324,334	687.7 (± 275.47)	675.3 (± 274.46)		

Notes:

[9] - ITT-E Population.

[10] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in CD4+ cell counts at Week 24 and 48

End point title	Changes from Baseline in CD4+ cell counts at Week 24 and 48

End point description:

CD4+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Blood samples were collected at specified time points to assess CD4+. It was evaluated by flow cytometry. Baseline value is defined as the the latest pre-dose assessment (Day 1). Change from Baseline was defined as post-dose visit value minus Baseline value. Adjusted mean and standard error has been presented. Adjusted mean is the estimated mean change from Baseline at each visit in each arm calculated from a repeated measures model adjusting for the following covariates/factors: treatment, visit, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, treatment and visit interaction, and Baseline CD4+ cell count and visit interaction, with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[11]	358[12]		
Units: Cells per cubic millimeter				
arithmetic mean (standard error)				
Week 24, n=340,341	192.2 (± 9.67)	175.1 (± 9.41)		
Week 48, n=324,334	222.2 (± 9.87)	217.7 (± 10.64)		

Notes:

[11] - ITT-E Population

[12] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 24. Following covariates/factors were adjusted: treatment, visit, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, treatment and visit interaction and Baseline CD4+ cell count and visit interaction with visit as the repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.206
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (net)
Point estimate	17.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.4
upper limit	43.6

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 48. Following covariates/factors were adjusted: treatment, visit, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, treatment and visit interaction and Baseline CD4+ cell count and visit interaction with visit as the repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.754
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (net)
Point estimate	4.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	33

Secondary: Number of participants with HIV-1 Disease Progression

End point title	Number of participants with HIV-1 Disease Progression

End point description:

HIV-associated conditions were recorded during the study and was assessed according to the 2014 Centers for Disease Control and Prevention (CDC) Classification System for HIV Infection in Adults. Disease progression summarize participants who had HIV infection stage 3 associated conditions or death. Indicators of clinical disease progression were defined as: CDC Category Stage 1 at enrolment to Stage 3 event; CDC Category Stage 2 at enrolment to Stage 3 event; CDC Category Stage 3 at enrolment to New Stage 3 Event; CDC Category Stage 1, 2 or 3 at enrolment to Death.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[13]	358[14]		
Units: Participants				
No HIV-1 disease progression	352	356		
From CDC Stage 1 to CDC Stage 3 Event	0	0		
From CDC Stage 2 to CDC Stage 3 Event	2	2		
From CDC Stage 3 to New CDC Stage 3 Event	2	0		
From CDC Stage 1, 2 or 3 to Death	0	0		

Notes:

[13] - ITT-E Population

[14] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent genotypic resistance

End point title	Number of participants with treatment-emergent genotypic

	resistance

End point description:

Number of participants, who meet confirmed virologic withdrawal (CVW) criteria, with treatment emergent phenotypic resistance to Integrase strand transfer inhibitor (INSTI) and/or Nucleoside reverse transcriptase inhibitor (NRTI) was summarized. The Viral Genotypic Population comprised of all participants in the ITT-E population who have available on-treatment genotypic resistance data. Only those participants available at the specified time points were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[15]	2[16]		
Units: Participants				
INSTI Mutations	0	0		
Major mutations of NRTI	0	0		

Notes:

[15] - Viral Genotypic Population

[16] - Viral Genotypic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent phenotypic resistance

End point title	Number of participants with treatment-emergent phenotypic resistance

End point description:

Number of participants, who meet CVW criteria, with treatment emergent phenotypic resistance to INSTI and/or NRTI were summarized. Assessment of antiviral activity of anti-retroviral therapy (ART) using phenotypic test results was interpreted through a proprietary algorithm (from Monogram Biosciences) and provides the overall susceptibility of the drug. Partially sensitive and resistant calls were considered resistant in this analysis. Number of participants with phenotype at time of CVW by phenotypic cut-off at or prior to Week 48 have been presented. The Viral Phenotypic Population comprised of all participants in the ITT-E population who have available on-treatment phenotypic resistance data. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4[17]	2[18]		
Units: Participants				
INSTI, DTG, Sensitive, n=4,1	4	1		
INSTI, DTG, Resistant, n=4,1	0	0		

INSTI, EVG, Sensitive, n=4,1	4	1		
INSTI, EVG, Resistant, n=4,1	0	0		
INSTI, RAL, Sensitive, n=4,1	4	1		
INSTI, RAL, Resistant, n=4,1	0	0		
NRTI, 3TC, Sensitive, n=4,2	4	2		
NRTI, 3TC, Resistant, n=4,2	0	0		
NRTI, ABC, Sensitive, n=4,2	4	2		
NRTI, ABC, Resistant, n=4,2	0	0		
NRTI, AZT, Sensitive, n=4,2	4	2		
NRTI, AZT, Resistant, n=4,2	0	0		
NRTI, D4T, Sensitive, n=4,2	4	2		
NRTI, D4T, Resistant, n=4,2	0	0		
NRTI, DDI, Sensitive, n=4,2	4	2		
NRTI, DDI, Resistant, n=4,2	0	0		
NRTI, FTC, Sensitive, n=4,2	4	2		
NRTI, FTC, Resistant, n=4,2	0	0		
NRTI, TDF, Sensitive, n=4,2	4	2		
NRTI, TDF, Resistant, n=4,2	0	0		

Notes:

[17] - Viral Phenotypic Population

[18] - Viral Phenotypic Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any adverse event (AE) and serious AE (SAE)

End point title	Number of participants with any adverse event (AE) and serious AE (SAE)

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention or event associated with liver injury and impaired liver function were categorized as SAE. Safety Population was used which comprised of all participants who received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[19]	358[20]		
Units: Participants				
Any AE	276	295		
Any SAE	21	22		

Notes:

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs by their severity grades

End point title	Number of participants with AEs by their severity grades

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Adverse events were evaluated by the investigator and graded according to the Division of Acquired Immunodeficiency Syndrome (DAIDS) toxicity scales from Grade 1 to 5 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening, 5=Death). The higher the grade, the more severe the symptoms. Number of participants with adverse events by maximum grade have been presented.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[21]	358[22]		
Units: Participants				
Grade 1 AEs	60	61		
Grade 2 AEs	195	210		
Grade 3 AEs	19	22		
Grade 4 AEs	2	2		
Grade 5 AEs	0	0		

Notes:

[21] - Safety Population

[22] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any drug related AEs and drug related AEs by maximum grade

End point title	Number of participants with any drug related AEs and drug related AEs by maximum grade

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Adverse events were evaluated by the investigator and graded according to the DAIDS toxicity scales from Grade 1 to 5 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening, 5=Death). The higher the grade, the more severe the symptoms. Number of participants with drug related AEs and drug related AEs by maximum grade have been presented.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[23]	358[24]		
Units: Participants				
Any drug related AE	71	94		
Drug related AEs with maximum toxicity Grade 1	50	69		
Drug related AEs with maximum toxicity Grade 2	18	22		
Drug related AEs with maximum toxicity Grade 3	3	3		
Drug related AEs with maximum toxicity Grade 4	0	0		
Drug related AEs with maximum toxicity Grade 5	0	0		

Notes:

[23] - Safety Population

[24] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-Baseline emergent hematology toxicities

End point title	Number of participants with maximum post-Baseline emergent hematology toxicities

End point description:

Blood samples were collected up to Week 48 for assessment of hematology parameters to assess any abnormality per toxicity scales for platelet count, neutrophils, hemoglobin. Any abnormality was graded according to DAIDS toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). The higher the grade, the more severe the symptoms. Only those participants with maximum post-Baseline emergent hematology toxicities in any of the hematology parameters have been presented.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[25]	358[26]		
Units: Participants				
Hemoglobin, Grades 1 to 4	7	5		
Hemoglobin, Grades 2 to 4	1	1		

Hemoglobin, Grades 3 to 4	0	0		
Hemoglobin, Grade 1	6	4		
Hemoglobin, Grade 2	1	1		
Hemoglobin, Grade 3	0	0		
Hemoglobin, Grade 4	0	0		
Leukocytes, Grades 1 to 4	5	3		
Leukocytes, Grades 2 to 4	2	2		
Leukocytes, Grades 3 to 4	0	0		
Leukocytes, Grade 1	3	1		
Leukocytes, Grade 2	2	2		
Leukocytes, Grade 3	0	0		
Leukocytes, Grade 4	0	0		
Neutrophils, Grades 1 to 4	16	12		
Neutrophils, Grades 2 to 4	10	5		
Neutrophils, Grades 3 to 4	3	2		
Neutrophils, Grade 1	6	7		
Neutrophils, Grade 2	7	3		
Neutrophils, Grade 3	2	2		
Neutrophils, Grade 4	1	0		
Platelets, Grades 1 to 4	9	9		
Platelets, Grades 2 to 4	3	4		
Platelets, Grades 3 to 4	0	1		
Platelets, Grade 1	6	5		
Platelets, Grade 2	3	3		
Platelets, Grade 3	0	1		
Platelets, Grade 4	0	0		

Notes:

[25] - Safety Population

[26] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-Baseline emergent chemistry toxicities

End point title	Number of participants with maximum post-Baseline emergent chemistry toxicities

End point description:

Blood samples were collected up to Week 48 for assessment of Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST), Creatinine, Glucose, Potassium, Sodium, Chloride, Calcium, Total carbon dioxide (CO2), Alkaline phosphatase (ALP), Phosphate, Total bilirubin, Total protein, Albumin, Creatine phosphokinase (CPK), Creatinine clearance,Glomerular filtration rate (GFR), Total cholesterol, High density lipoprotein (HDL), Low density lipoprotein (LDL), Triglyceride and Lipase. Any abnormality was graded according to DAIDS toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). The higher the grade, the more severe the symptoms. Only those participants with maximum post-Baseline emergent chemistry toxicities in any of the chemistry parameters have been presented.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[27]	358[28]		
Units: Participants				
ALT, Grades 1 to 4	31	48		
ALT, Grades 2 to 4	14	16		
ALT, Grades 3 to 4	9	8		
ALT, Grade 1	17	32		
ALT, Grade 2	5	8		
ALT, Grade 3	4	3		
ALT, Grade 4	5	5		
Albumin, Grades 1 to 4	1	1		
Albumin, Grades 2 to 4	1	0		
Albumin, Grades 3 to 4	0	0		
Albumin, Grade 1	0	1		
Albumin, Grade 2	1	0		
Albumin, Grade 3	0	0		
Albumin, Grade 4	0	0		
ALP, Grades 1 to 4	7	7		
ALP, Grades 2 to 4	3	1		
ALP, Grades 3 to 4	0	0		
ALP, Grade 1	4	6		
ALP, Grade 2	3	1		
ALP, Grade 3	0	0		
ALP, Grade 4	0	0		
AST, Grades 1 to 4	35	51		
AST, Grades 2 to 4	17	20		
AST, Grades 3 to 4	5	12		
AST, Grade 1	18	31		
AST, Grade 2	12	8		
AST, Grade 3	4	8		
AST, Grade 4	1	4		
Bilirubin, Grades 1 to 4	28	37		
Bilirubin, Grades 2 to 4	8	13		
Bilirubin, Grades 3 to 4	4	4		
Bilirubin, Grade 1	20	24		
Bilirubin, Grade 2	4	9		
Bilirubin, Grade 3	2	4		
Bilirubin, Grade 4	2	0		
CO2, Grades 1 to 4	99	81		
CO2, Grades 2 to 4	7	6		
CO2, Grades 3 to 4	0	0		
CO2, Grade 1	92	75		
CO2, Grade 2	7	6		
CO2, Grade 3	0	0		
CO2, Grade 4	0	0		
Cholesterol, Grades 1 to 4	55	27		
Cholesterol, Grades 2 to 4	19	9		
Cholesterol, Grades 3 to 4	0	0		
Cholesterol, Grade 1	36	18		
Cholesterol, Grade 2	19	9		

Cholesterol, Grade 3	0	0		
Cholesterol, Grade 4	0	0		
CPK, Grades 1 to 4	42	40		
CPK, Grades 2 to 4	24	28		
CPK, Grades 3 to 4	13	18		
CPK, Grade 1	18	12		
CPK, Grade 2	11	10		
CPK, Grade 3	8	11		
CPK, Grade 4	5	7		
Creatinine, Grades 1 to 4	15	22		
Creatinine, Grades 2 to 4	1	2		
Creatinine, Grades 3 to 4	0	1		
Creatinine, Grade 1	14	20		
Creatinine, Grade 2	1	1		
Creatinine, Grade 3	0	1		
Creatinine, Grade 4	0	0		
Direct Bilirubin, Grades 1 to 4	10	9		
Direct Bilirubin, Grades 2 to 4	10	9		
Direct Bilirubin, Grades 3 to 4	10	9		
Direct Bilirubin, Grade 1	0	0		
Direct Bilirubin, Grade 2	0	0		
Direct Bilirubin, Grade 3	10	9		
Direct Bilirubin, Grade 4	0	0		
GFR, Grades 1 to 4	151	185		
GFR, Grades 2 to 4	151	185		
GFR, Grades 3 to 4	9	18		
GFR, Grade 1	0	0		
GFR, Grade 2	142	167		
GFR, Grade 3	9	17		
GFR, Grade 4	0	1		
Hypercalcaemia, Grades 1 to 4	3	2		
Hypercalcaemia, Grades 2 to 4	0	0		
Hypercalcaemia, Grades 3 to 4	0	0		
Hypercalcaemia, Grade 1	3	2		
Hypercalcaemia, Grade 2	0	0		
Hypercalcaemia, Grade 3	0	0		
Hypercalcaemia, Grade 4	0	0		
Hyperglycemia, Grades 1 to 4	59	50		
Hyperglycemia, Grades 2 to 4	23	13		
Hyperglycemia, Grades 3 to 4	3	2		
Hyperglycemia, Grade 1	36	37		
Hyperglycemia, Grade 2	20	11		
Hyperglycemia, Grade 3	3	2		
Hyperglycemia, Grade 4	0	0		
Hyperkalemia, Grades 1 to 4	0	0		
Hyperkalemia, Grades 2 to 4	0	0		
Hyperkalemia, Grades 3 to 4	0	0		
Hyperkalemia, Grade 1	0	0		
Hyperkalemia, Grade 2	0	0		
Hyperkalemia, Grade 3	0	0		
Hyperkalemia, Grade 4	0	0		
Hypernatremia, Grades 1 to 4	3	0		

Hypernatremia, Grades 2 to 4	0	0		
Hypernatremia, Grades 3 to 4	0	0		
Hypernatremia, Grade 1	3	0		
Hypernatremia, Grade 2	0	0		
Hypernatremia, Grade 3	0	0		
Hypernatremia, Grade 4	0	0		
Hypocalcaemia, Grades 1 to 4	9	3		
Hypocalcaemia, Grades 2 to 4	1	0		
Hypocalcaemia, Grades 3 to 4	0	0		
Hypocalcaemia, Grade 1	8	3		
Hypocalcaemia, Grade 2	1	0		
Hypocalcaemia, Grade 3	0	0		
Hypocalcaemia, Grade 4	0	0		
Hypoglycemia, Grades 1 to 4	13	13		
Hypoglycemia, Grades 2 to 4	7	3		
Hypoglycemia, Grades 3 to 4	2	1		
Hypoglycemia, Grade 1	6	10		
Hypoglycemia, Grade 2	5	12		
Hypoglycemia, Grade 3	1	0		
Hypoglycemia, Grade 4	1	1		
Hypokalemia, Grades 1 to 4	2	5		
Hypokalemia, Grades 2 to 4	0	1		
Hypokalemia, Grades 3 to 4	0	0		
Hypokalemia, Grade 1	2	4		
Hypokalemia, Grade 2	0	1		
Hypokalemia, Grade 3	0	0		
Hypokalemia, Grade 4	0	0		
Hyponatremia, Grades 1 to 4	19	21		
Hyponatremia, Grades 2 to 4	1	0		
Hyponatremia, Grades 3 to 4	0	0		
Hyponatremia, Grade 1	18	21		
Hyponatremia, Grade 2	1	0		
Hyponatremia, Grade 3	0	0		
Hyponatremia, Grade 4	0	0		
LDL Cholesterol, Grades 1 to 4	41	25		
LDL Cholesterol, Grades 2 to 4	14	10		
LDL Cholesterol, Grades 3 to 4	5	3		
LDL Cholesterol, Grade 1	27	15		
LDL Cholesterol, Grade 2	9	7		
LDL Cholesterol, Grade 3	5	3		
LDL Cholesterol, Grade 4	0	0		
Lactate Dehydrogenase, Grades 1 to 4	3	4		
Lactate Dehydrogenase, Grades 2 to 4	0	1		
Lactate Dehydrogenase, Grades 3 to 4	0	0		
Lactate Dehydrogenase, Grade 1	3	3		
Lactate Dehydrogenase, Grade 2	0	1		
Lactate Dehydrogenase, Grade 3	0	0		
Lactate Dehydrogenase, Grade 4	0	0		
Lipase, Grades 1 to 4	41	50		
Lipase, Grades 2 to 4	23	25		
Lipase, Grades 3 to 4	5	9		
Lipase, Grade 1	18	25		

Lipase, Grade 2	18	16		
Lipase, Grade 3	4	4		
Lipase, Grade 4	1	5		
Phosphate, Grades 1 to 4	40	47		
Phosphate, Grades 2 to 4	19	31		
Phosphate, Grades 3 to 4	1	3		
Phosphate, Grade 1	21	16		
Phosphate, Grade 2	18	28		
Phosphate, Grade 3	1	3		
Phosphate, Grade 4	0	0		
Triglycerides, Grades 1 to 4	56	44		
Triglycerides, Grades 2 to 4	11	10		
Triglycerides, Grades 3 to 4	6	3		
Triglycerides, Grade 1	45	34		
Triglycerides, Grade 2	5	7		
Triglycerides, Grade 3	5	2		
Triglycerides, Grade 4	1	1		

Notes:

[27] - Safety Population

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinue treatment due to AEs over Weeks 24, 48

End point title	Number of participants who discontinue treatment due to AEs over Weeks 24, 48

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Data cut-off dates for analysis at Week 24 and Week 48 were 19-Jan-2018 and 22-May-2018 respectively. Number of participants who discontinued treatment due to AEs have been reported.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[29]	358[30]		
Units: Participants				
Up to Week 24	6	4		
Up to Week 48	7	8		

Notes:

[29] - Safety Population

[30] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in renal biomarkers-Serum Cystatin C and Serum Retinol Binding Protein (RBP) at Weeks 24, 48

End point title	Change from Baseline in renal biomarkers-Serum Cystatin C and Serum Retinol Binding Protein (RBP) at Weeks 24, 48

End point description:

Blood and/or urine were collected to perform evaluation of renal inflammation biomarkers which included Serum Cystatin C and Serum Retinol Binding Protein (RBP). Baseline value is the latest pre-dose assessment. Change from Baseline was defined as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented. Adjusted mean is the estimated mean change from baseline at each visit in each arm calculated from a repeated measures model adjusting for: treatment, visit, baseline plasma HIV-1 RNA (factor), baseline CD4+ cell count (factor), age, sex (factor), race (factor), presence of diabetes mellitus (factor), presence of hypertension (factor), baseline biomarker value, treatment and visit interaction, and baseline biomarker value and visit interaction; with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[31]	358[32]		
Units: Milligrams per Liter (mg/L)				
arithmetic mean (standard error)				
Serum Cystatin C, Week 24, n=338, 336	-0.05 (± 0.007)	-0.03 (± 0.007)		
Serum Cystatin C, Week 48, n=324, 332	-0.07 (± 0.007)	-0.04 (± 0.006)		
Serum RBP, Week 24, n=332, 334	1.6 (± 0.41)	1.9 (± 0.51)		
Serum RBP, Week 48, n=322, 332	0.5 (± 0.47)	0.6 (± 0.46)		

Notes:

[31] - Safety Population

[32] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Serum Cystatin C, Week 24

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.025
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Serum Cystatin C, Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.01

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Serum RBP, Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.683
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	1

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Serum RBP, Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.93
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.2

Secondary: Change from Baseline in renal biomarkers-Serum GFR from cystatin C Adjusted using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Serum or Plasma GFR from creatinine adjusted using CKD-EPI at Weeks 24, 48

End point title	Change from Baseline in renal biomarkers-Serum GFR from cystatin C Adjusted using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Serum or Plasma GFR from creatinine adjusted using CKD-EPI at Weeks 24, 48

End point description:

Blood and/or urine were collected for evaluation of renal inflammation biomarkers-Serum GFR from cystatin C adjusted using CKD-EPI (GFR-cystatin C adjusted)and Serum/Plasma GFR from creatinine adjusted using CKD-EPI. Baseline value is the latest pre-dose assessment. Change from Baseline was defined as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented. Adjusted mean is the estimated mean change from baseline at each visit in each arm calculated from a repeated measures model adjusting for: treatment, visit, baseline plasma HIV-1 RNA(factor), baseline CD4+ cell count(factor), age, sex(factor), race(factor), presence of diabetes mellitus(factor), presence of hypertension(factor), baseline biomarker value, treatment and visit interaction, and baseline biomarker value and visit interaction; with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[33]	358[34]		
Units: Milliliter/minute/1.73*meter^2				
arithmetic mean (standard error)				
GFR-cystatin C adjusted, Week 24, n=338, 336	4.4 (± 0.63)	2.2 (± 0.60)		
GFR-cystatin C adjusted, Week 48, n=324, 332	7.0 (± 0.60)	4.1 (± 0.59)		
GFR-creatinine adjusted, Week 24, n=340, 341	-13.5 (± 0.59)	-16.7 (± 0.56)		
GFR-creatinine adjusted, Week 48, n=326,335	-12.1 (± 0.56)	-15.6 (± 0.55)		

Notes:
[33] - Safety Population
[34] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: GFR-cystatin C adjusted, Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.011
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	4

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: GFR-cystatin C adjusted, Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.2
upper limit	4.5

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: GFR-creatinine adjusted, Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	4.8

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
GFR- creatinine adjusted, Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	5.1

Secondary: Change from Baseline in renal biomarker-Serum or Plasma Creatinine at Weeks 24, 48

End point title	Change from Baseline in renal biomarker-Serum or Plasma Creatinine at Weeks 24, 48

End point description:

Blood and/or urine were collected to perform evaluation of renal inflammation biomarker which included Serum or Plasma Creatinine. Baseline value is defined as the latest pre-dose assessment. Change from Baseline was calculated as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented. Adjusted mean is the estimated mean change from baseline at each visit in each arm calculated from a repeated measures model adjusting for: treatment, visit, baseline plasma HIV-1 RNA (factor), baseline CD4+ cell count (factor), age, sex (factor), race (factor), presence of diabetes mellitus (factor), presence of hypertension (factor), baseline biomarker value, treatment and visit interaction, and baseline biomarker value and visit interaction; with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[35]	358[36]		
Units: Micromoles per Liter (umol/L)				
arithmetic mean (standard error)				
Serum or Plasma Creatinine, Week 24, n=340, 343	11.88 (± 0.510)	15.07 (± 0.520)		
Serum or Plasma Creatinine, Week 48, n=326, 335	10.39 (± 0.466)	13.61 (± 0.480)		

Notes:

[35] - Safety Population

[36] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-3.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.62
upper limit	-1.75

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-3.22

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.54
upper limit	-1.91

Secondary: Ratio to Baseline in renal biomarkers-Urine and Serum Beta-2 Microglobulin (B2M), Urine Albumin/Creatinine, Urine B2M/Urine Creatinine, Urine Phosphate, Urine Protein/Creatinine, Urine RBP 4 and Urine RBP 4/Urine Creatinine at Weeks 24, 48

End point title	Ratio to Baseline in renal biomarkers-Urine and Serum Beta-2 Microglobulin (B2M), Urine Albumin/Creatinine, Urine B2M/Urine Creatinine, Urine Phosphate, Urine Protein/Creatinine, Urine RBP 4 and Urine RBP 4/Urine Creatinine at Weeks 24, 48

End point description:

Blood and/or urine were collected to perform evaluation of renal inflammation biomarkers which included Urine and Serum B2M, Urine Albumin/Creatinine, Urine B2M/Urine Creatinine, Urine Phosphate, Urine Protein/Creatinine, Urine RBP 4 and Urine RBP 4/Urine Creatinine. Baseline value is defined as the latest pre-dose assessment. Ratio to Baseline was calculated as ratio of post-dose visit value over Baseline value. Statistical analysis of changes from baseline were performed on log-transformed data. Results were transformed back via exponential transformation such that treatment comparisons are assessed via odds ratios. Estimated ratio of geometric means (each visit over Baseline) and 95% confidence interval (CI) have been presented. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[37]	358[38]		
Units: Ratio				
geometric mean (confidence interval 95%)				
Serum B2M, Week 24, n=338, 335	0.798 (0.779 to 0.817)	0.872 (0.856 to 0.890)		
Serum B2M, Week 48, n=324, 332	0.806 (0.790 to 0.823)	0.892 (0.876 to 0.908)		
Urine B2M, Week 24, n=121, 95	0.887 (0.756 to 1.039)	1.351 (1.060 to 1.722)		
Urine B2M, Week 48, n=119, 103	0.900 (0.792 to 1.022)	1.338 (1.148 to 1.560)		
Urine Albumin/Creatinine, Week 24, n=254, 252	1.014 (0.927 to 1.109)	1.050 (0.964 to 1.144)		
Urine Albumin/Creatinine , Week 48, n=237, 244	0.934 (0.857 to 1.017)	1.048 (0.968 to 1.134)		
Urine B2M/Urine Creatinine , Week 24, n=121, 95	0.852 (0.737 to 0.985)	1.331 (1.071 to 1.655)		
Urine B2M/Urine Creatinine , Week 48, n=114, 100	0.888 (0.777 to 1.015)	1.278 (1.119 to 1.458)		
Urine Phosphate, Week 24, n=330, 332	1.115 (1.025 to 1.212)	1.012 (0.934 to 1.095)		

Urine Phosphate , Week 48, n=316, 330	1.061 (0.983 to 1.145)	1.075 (0.996 to 1.159)		
Urine Protein/Creatinine , Week 24, n=269, 265	0.850 (0.806 to 0.895)	1.016 (0.960 to 1.075)		
Urine Protein/Creatinine , Week 48, n=252, 269	0.879 (0.838 to 0.922)	1.061 (1.009 to 1.115)		
Urine RBP 4, Week 24, n=332, 330	0.934 (0.842 to 1.036)	1.073 (0.951 to 1.209)		
Urine RBP 4, Week 48, n=318, 328	1.115 (1.009 to 1.233)	1.490 (1.332 to 1.667)		
Urine RBP 4/Urine Creatinine , Week 24, n=329, 330	0.919 (0.846 to 0.998)	1.110 (1.003 to 1.228)		
Urine RBP 4/Urine Creatinine , Week 48, n=304, 318	1.147 (1.060 to 1.241)	1.500 (1.367 to 1.646)		

Notes:

[37] - Safety Population

[38] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 24. Serum B2M	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.915
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.887
upper limit	0.943

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 48. Serum B2M	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.904

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	0.929

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Week 24. Urine B2M	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.656
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.491
upper limit	0.877

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Week 48. Urine B2M	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.672
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.551
upper limit	0.821

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Week 24. Urine Albumin/Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.575
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.965
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.853
upper limit	1.092

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Week 48. Urine Albumin/Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.051
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.891
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.793
upper limit	1.001

Statistical analysis title	Statistical Analysis 7
Statistical analysis description: Week 24. Urine B2M/Urine Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.493
upper limit	0.831

Statistical analysis title	Statistical Analysis 8
Statistical analysis description: Week 48. Urine B2M/Urine Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.695
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.576
upper limit	0.839

Statistical analysis title	Statistical Analysis 9
Statistical analysis description: Week 24. Urine Phosphate	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.099
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	1.102
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.982
upper limit	1.237

Statistical analysis title	Statistical Analysis 10
Statistical analysis description: Week 48. Urine Phosphate	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.816
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.987
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.886
upper limit	1.1

Statistical analysis title	Statistical Analysis 11
Statistical analysis description: Week 24. Urine Protein/Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.836
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.774
upper limit	0.904

Statistical analysis title	Statistical Analysis 12
Statistical analysis description: Week 48. Urine Protein/Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.829
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.773
upper limit	0.888

Statistical analysis title	Statistical Analysis 13
Statistical analysis description: Week 24. Urine RBP 4	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.087
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.871
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.743
upper limit	1.02

Statistical analysis title	Statistical Analysis 14
Statistical analysis description: Week 48. Urine RBP 4	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.748
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.644
upper limit	0.87

Statistical analysis title	Statistical Analysis 15
Statistical analysis description: Week 24. Urine RBP 4/Urine Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.828
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.727
upper limit	0.944

Statistical analysis title	Statistical Analysis 16
Statistical analysis description:	
Week 48. Urine RBP 4/Urine Creatinine	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Ratio of geometric means
Point estimate	0.765
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.677
upper limit	0.864

Secondary: Change from Baseline in bone biomarkers-Serum Bone Specific Alkaline Phosphatase (bone-ALP), Serum Osteocalcin, Serum Procollagen 1 N-Terminal Propeptide (PINP) and Serum Type I Collagen C-Telopeptides (CTX-1) at Weeks 24, 48

End point title	Change from Baseline in bone biomarkers-Serum Bone Specific Alkaline Phosphatase (bone-ALP), Serum Osteocalcin, Serum Procollagen 1 N-Terminal Propeptide (PINP) and Serum Type I Collagen C-Telopeptides (CTX-1) at Weeks 24, 48

End point description:

Blood samples were collected to perform evaluation of bone biomarkers which included bone-ALP, Serum Osteocalcin, PINP and CTX-1. Baseline value is defined as the latest pre-dose assessment. Change from Baseline was calculated as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented. Adjusted mean is the estimated mean change from baseline at each visit in each arm calculated from a repeated measures model adjusting for: treatment, visit, baseline plasma HIV-1 RNA (factor), baseline CD4+ cell count (factor), age, sex (factor), race (factor), BMI (factor), smoking status (factor), current Vitamin D use (factor), baseline biomarker value, treatment and visit interaction, and baseline biomarker value and visit interaction; with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:
Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[39]	358[40]		
Units: Micrograms per Liter (ug/L)				
arithmetic mean (standard error)				
Bone-ALP, Week 24, n=334, 332	0.91 (± 0.179)	3.13 (± 0.199)		
Bone-ALP, Week 48, n=321, 331	1.21 (± 0.193)	3.79 (± 0.239)		
Serum Osteocalcin, Week 24, n=335, 334	2.56 (± 0.341)	6.74 (± 0.347)		
Serum Osteocalcin, Week 48, n=322, 330	0.78 (± 0.311)	6.01 (± 0.400)		
PINP, Week 24, n=337, 336	4.5 (± 0.91)	18.3 (± 1.06)		
PINP, Week 48, n=321, 334	0.5 (± 0.83)	13.1 (± 0.84)		
CTX-1, Week 24, n=337, 334	0.1192 (± 0.01304)	0.2820 (± 0.01472)		
CTX-1, Week 48, n=323, 331	0.1338 (± 0.01258)	0.3352 (± 0.01885)		

Notes:
[39] - Safety Population
[40] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 24. Bone ALP	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-2.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.75
upper limit	-1.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 48. Bone ALP	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-2.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.19
upper limit	-1.98

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Week 28. Serum Osteocalcin	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-4.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.15
upper limit	-3.23

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Week 48. Serum Osteocalcin	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-5.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.22
upper limit	-4.23

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Week 24. Serum PINP	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-13.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.5
upper limit	-11.1

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Week 48. Serum PINP	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-12.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	-10.3

Statistical analysis title	Statistical Analysis 7
Statistical analysis description: Week 24. CTX-1	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.1628
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2015
upper limit	-0.1241

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Week 48. CTX-1	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.2015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.246
upper limit	-0.1569

Secondary: Change from Baseline in bone biomarker-Serum Vitamin D at Weeks 24, 48

End point title	Change from Baseline in bone biomarker-Serum Vitamin D at Weeks 24, 48

End point description:

Blood samples were collected to perform evaluation of bone biomarker serum vitamin D. Baseline value is defined as the latest pre-dose assessment. Change from Baseline was calculated as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented. Adjusted mean is the estimated mean change from baseline at each visit in each arm calculated from a repeated measures model adjusting for: treatment, visit, baseline plasma HIV-1 RNA (factor), baseline CD4+ cell count (factor), age, sex (factor), race (factor), BMI (factor), smoking status (factor), current Vitamin D use (factor), baseline biomarker value, treatment and visit interaction, and baseline biomarker value and visit interaction; with visit as the repeated factor. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[41]	358[42]		
Units: Nanomoles per Liter (nmol/L)				
arithmetic mean (standard error)				
Serum Vitamin D, Week 24, n=337, 337	5.9 (± 1.15)	12.4 (± 1.33)		
Serum Vitamin D, Week 48, n=322, 333	-3.1 (± 0.89)	3.1 (± 1.10)		

Notes:

[41] - Safety Population

[42] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.9
upper limit	-3

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-6.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	-9
upper limit	-3.4

Secondary: Percentage change from Baseline in fasting lipids-Serum or Plasma Cholesterol, Serum or Plasma HDL Cholesterol (Direct), Serum or Plasma LDL Cholesterol (Calculated or Direct) and Serum or Plasma Triglycerides at Weeks 24, 48

End point title	Percentage change from Baseline in fasting lipids-Serum or Plasma Cholesterol, Serum or Plasma HDL Cholesterol (Direct), Serum or Plasma LDL Cholesterol (Calculated or Direct) and Serum or Plasma Triglycerides at Weeks 24, 48

End point description:

Blood samples were collected to perform evaluation of fasting lipids which included Serum or Plasma Cholesterol, Serum or Plasma HDL Cholesterol (Direct), Serum or Plasma LDL Cholesterol (Calculated or Direct) and Serum or Plasma Triglycerides. Baseline value is defined as the latest pre-dose assessment (Day 1). Percentage change from Baseline was calculated as 100 multiplied by ([post-dose visit value minus Baseline value] divided by Baseline value). Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[43]	358[44]		
Units: Percentage change				
arithmetic mean (standard deviation)				
Serum or Plasma Cholesterol, Week 24, n=294, 297	9.4 (± 17.44)	-4.7 (± 16.12)		
Serum or Plasma Cholesterol, Week 48, n=280, 289	10.5 (± 18.89)	-2.4 (± 17.14)		
HDL Cholesterol, Direct, Week 24, n=294, 297	16.4 (± 22.58)	3.4 (± 21.55)		
HDL Cholesterol, Direct, Week 48, n=280, 289	15.0 (± 25.07)	5.0 (± 33.04)		
LDL Cholesterol, Week 24, n=294, 297	12.4 (± 45.05)	-8.1 (± 23.70)		
LDL Cholesterol, Week 48, n=280, 289	14.8 (± 48.74)	-4.0 (± 24.06)		
Triglycerides ,Week 24, n=294, 297	8.5 (± 46.57)	4.3 (± 72.35)		
Triglycerides , Week 48, n=280, 289	12.8 (± 68.99)	4.4 (± 70.43)		

Notes:

[43] - Safety Population

[44] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from Baseline in fasting lipid-Serum or Plasma Total Cholesterol/HDL Cholesterol Ratio at Weeks 24, 48

End point title	Percentage change from Baseline in fasting lipid-Serum or Plasma Total Cholesterol/HDL Cholesterol Ratio at Weeks 24, 48

End point description:

Blood samples were collected to perform evaluation of fasting lipid-Serum or Plasma Total Cholesterol/HDL Cholesterol Ratio. Baseline value is the latest pre-dose assessment (Day 1). Percentage change from Baseline was calculated as 100 multiplied by ([post-dose visit value minus Baseline value] divided by Baseline value). Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[45]	358[46]		
Units: Percentage change				
arithmetic mean (standard deviation)				
Total/HDL Cholesterol Ratio, Week 24, n=294, 297	-4.0 (± 19.08)	-4.6 (± 27.52)		
Total/HDL Cholesterol Ratio, Week 48, n=280, 289	-0.2 (± 31.10)	-4.4 (± 16.96)		

Notes:

[45] - Safety Population

[46] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with Grade 2 or greater laboratory abnormalities in fasting LDL cholesterol by Weeks 24, 48

End point title	Percentage of participants with Grade 2 or greater laboratory abnormalities in fasting LDL cholesterol by Weeks 24, 48

End point description:

Blood samples were collected to perform evaluation of fasting LDL cholesterol. Any abnormalities were evaluated by the investigator and graded according to DAIDS toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). The higher the grade, the more severe the symptoms. Percentage of participants with Grade 2 or greater laboratory abnormalities in fasting LDL cholesterol by Weeks 24 and 48 have been presented. Participants without any post-Baseline fasting LDL cholesterol value prior to Week 48 or those who had Baseline lipids-lowering agents are not included. Lipid Last Observation Carried Forward (LOCF) data was used such that the last available fasted, on-treatment lipid value prior to the initiation of a lipid-lowering agent was used in place of future observed values. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[47]	358[48]		
Units: Percentage of participants				
Week 24, n=309, 316	4	2		
Week 48, n=318, 320	4	3		

Notes:

[47] - Safety Population

[48] - Safety Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.157 [49]
Method	Fisher exact
Parameter estimate	Difference in percentage
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	4.6

Notes:

[49] - Fisher's exact p-value.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.414 [50]
Method	Fisher exact
Parameter estimate	Difference in percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7
upper limit	4.2

Notes:

[50] - Fisher's exact p-value.

Secondary: Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count, Baseline HIV-1 RNA, race) with plasma HIV-1 RNA <50 c/mL at Week 24

End point title	Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count, Baseline HIV-1 RNA, race) with plasma HIV-1 RNA <50 c/mL at Week 24

End point description:

Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count, Baseline HIV-1 RNA, race) with HIV-1 RNA<50 c/mL was obtained using FDA Snapshot algorithm. The Snapshot algorithm treated 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 switch their concomitant ART prior to the visit of interest. Data was presented by subgroups: age (<35, 35 to <50, >=50 years); gender (males and females), Baseline CD4+ cell count (<=200, >200), Baseline HIV-1 RNA (<=100000, >100000) and Race (White, African American/African H., Asian, Other). Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Week 24

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[51]	358[52]		
Units: Percentage of participants				
Baseline CD4+ cell count, <=200,n=31,29	90	86		
Baseline CD4+ cell count, >200,n=325,329	93	94		
Female, n=59, 52	93	96		
Male, n=297, 306	92	92		
Age, <35,n= 211, 205	93	95		
Age, 35 to <50,n=116, 107	91	93		
Age, >=50, n=29, 46	93	85		
Baseline plasma HIV-1 RNA, <=100000,n=282,282	93	95		
Baseline plasma HIV-1 RNA, >100000,n=74, 76	92	87		
Race, White, n=243,248	93	95		
Race, African American/African H., n=44, 36	93	81		
Race, Asian, n=37, 42	89	93		
Race, Other, n=32, 32	94	94		

Notes:

[51] - ITT-E Population

[52] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count Baseline HIV-1 RNA, race) with plasma HIV-1 RNA <50 c/mL at Week 48

End point title	Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count Baseline HIV-1 RNA, race) with

	plasma HIV-1 RNA <50 c/mL at Week 48

End point description:

Percentage of participants by subgroups (by age, gender, Baseline CD4+ cell count, Baseline HIV-1 RNA, race) with HIV-1 RNA<50 c/mL was obtained using FDA Snapshot algorithm. The Snapshot algorithm treated 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 switch their concomitant ART prior to the visit of interest. Data was presented by subgroups: age (<35, 35 to <50, >=50 years); gender (males and females), Baseline CD4+ cell count (<=200, >200), Baseline HIV-1 RNA (<=100000, >100000) and Race (White, African American/African H., Asian, Other). Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[53]	358[54]		
Units: Percentage of participants				
Baseline CD4+ cell count, <=200,n=31,29	81	90		
Baseline CD4+ cell count, >200,n=325,329	91	93		
Female, n=59, 52	88	94		
Male, n=297, 306	90	92		
Age, <35,n= 211, 205	92	93		
Age, 35 to <50,n=116, 107	86	94		
Age, >=50, n=29, 46	90	87		
Baseline plasma HIV-1 RNA, <=100000,n=282,282	90	93		
Baseline plasma HIV-1 RNA, >100000,n=74, 76	88	91		
Race, White, n=243,248	90	94		
Race, African American/African H., n=44, 36	89	81		
Race, Asian, n=37, 42	92	98		
Race, Other, n=32, 32	88	94		

Notes:

[53] - ITT-E Population

[54] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Changes from Baseline in CD4+ cell counts at Week 48 by subgroups

End point title	Changes from Baseline in CD4+ cell counts at Week 48 by subgroups

End point description:

CD4+ cells are type of white blood cells that fight infection. Blood samples were collected at specified time points to assess CD4+. It was evaluated by flow cytometry. Baseline value is the latest pre-dose assessment (Day 1). Change from Baseline was defined as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented for subgroups (Baseline plasma HIV-1 RNA, Baseline CD4+ cell count, Age group, Gender and race). For each subgroup, adjusted mean is the estimated

mean change from Baseline in each arm calculated from Analysis of Covariance (ANCOVA) model adjusting for the following covariates/factors: treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, subgroup, and treatment and relevant subgroup interaction. For CD4+ cell count subgroup, Baseline CD4+ cell count group is included as a factor only. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[55]	358[56]		
Units: Cells per cubic millimeter				
arithmetic mean (standard error)				
Baseline plasma HIV-1 RNA,<=100000, n=257,264	220.0 (± 11.72)	212.4 (± 11.56)		
Baseline plasma HIV-1 RNA,>100000, n=67,70	238.5 (± 23.09)	235.5 (± 22.70)		
Baseline CD4+ cell count,<=200, n=26, 27	200.5 (± 36.97)	177.9 (± 36.18)		
Baseline CD4+ cell count,>200, n=298, 307	225.9 (± 10.84)	220.7 (± 10.68)		
Age group-1, <35,n= 194, 192	233.6 (± 13.49)	225.2 (± 13.53)		
Age group-1, 35 to <50, n=104, 101	208.7 (± 18.40)	211.2 (± 18.67)		
Age group-1, >=50, n=26, 41	212.6 (± 36.84)	194.8 (± 29.27)		
Female, n=54, 49	237.1 (± 25.53)	226.8 (± 26.98)		
Male, n=270, 285	221.2 (± 11.41)	215.6 (± 11.11)		
Race, White, n=223, 232	226.0 (± 12.58)	219.9 (± 12.37)		
Race, African Am/African H., n=38, 31	209.4 (± 30.54)	232.5 (± 33.79)		
Race, Asian, n=34, 41	246.4 (± 32.36)	197.2 (± 29.48)		
Race, Other, n=29, 30	200.0 (± 34.91)	208.1 (± 34.39)		

Notes:

[55] - ITT-E Population

[56] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Baseline plasma HIV-1 RNA,<=100000. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count and treatment and HIV-1 RNA interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.6
upper limit	39.8

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Baseline plasma HIV-1 RNA,>100000. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count and treatment and HIV-1 RNA interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-59.8
upper limit	65.9

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Baseline CD4+ cell count,<=200. Following covariates were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor),Baseline CD4+ cell count, and treatment and Baseline CD4+ cell count interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	22.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-78.3
upper limit	123.5

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Baseline CD4+ cell count,>200.
Following covariates were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, and treatment and Baseline CD4+ cell count interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.7
upper limit	35.1

Statistical analysis title	Statistical Analysis 5

Statistical analysis description:

Age<35. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	8.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.1
upper limit	45.9

Statistical analysis title	Statistical Analysis 6

Statistical analysis description:

Age 35 to <50. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-2.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.9
upper limit	48.9

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Age>=50. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	17.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.6
upper limit	110.1

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Female. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, gender, and treatment and gender interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	10.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-62.3
upper limit	83.1

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Male. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, gender, and treatment and gender interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	5.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.6
upper limit	36.9

Statistical analysis title	Statistical Analysis 10
Statistical analysis description:	
Race group white. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race group, and treatment and race group interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-28.5
upper limit	40.7

Statistical analysis title	Statistical Analysis 11
Statistical analysis description:	
Race group African Am/African H. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race group, and treatment and race group interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-112.6
upper limit	66.6

Statistical analysis title	Statistical Analysis 12
Statistical analysis description:	
Race group Asian. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race group, and treatment and race group interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	49.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-36.3
upper limit	134.7

Statistical analysis title	Statistical Analysis 13

Statistical analysis description:

Race group Other. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race group, and treatment and race group interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-8.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-104.1
upper limit	87.9

Secondary: Changes from Baseline in CD4+ cell counts at Week 24 by subgroups

End point title	Changes from Baseline in CD4+ cell counts at Week 24 by subgroups

End point description:

CD4+ cells are type of white blood cells that fight infection. Blood samples were collected at specified time points to assess CD4+. It was evaluated by flow cytometry. Baseline value is the latest pre-dose assessment (Day 1). Change from Baseline was defined as post-dose visit value minus Baseline value. Adjusted mean and standard error is presented for subgroups (Baseline plasma HIV-1 RNA, Baseline CD4+ cell count, Age, Gender, and race). For each subgroup, adjusted mean is the estimated mean change from Baseline in each arm calculated from ANCOVA model adjusting for the following covariates/factors: treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, subgroup, and treatment and relevant subgroup interaction. For CD4+ cell count subgroup, Baseline CD4+ cell count group is included as a factor only. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Week 24

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[57]	358[58]		
Units: Cells per cubic millimeter				
arithmetic mean (standard error)				
Baseline plasma HIV-1 RNA,<=100000, n=268,268	187.72 (± 10.860)	167.93 (± 10.842)		
Baseline plasma HIV-1 RNA,>100000, n=72,73	206.63 (± 21.107)	205.96 (± 20.990)		
Baseline CD4+ cell count,<=200, n=29,27	157.01 (± 33.113)	120.17 (± 34.151)		
Baseline CD4+ cell count,>200, n=311, 314	195.11 (± 10.026)	180.73 (± 9.972)		
Age, <35,n= 203,199	202.76 (± 12.456)	177.62 (± 12.563)		
Age, 35 to <50, n=109, 100	172.05 (± 16.983)	179.87 (± 17.733)		
Age, >=50, n=28, 42	188.79 (± 33.534)	159.34 (± 27.344)		
Female, n=57,50	199.45 (± 23.498)	181.78 (± 25.263)		
Male, n=283,291	190.21 (± 10.538)	175.05 (± 10.400)		
Race, White, n=235,236	204.36 (± 11.561)	180.49 (± 11.559)		
Race, African Am/African H., n=41,33	147.04 (± 27.706)	180.96 (± 30.880)		
Race, Asian, n=34, 41	169.92 (± 30.502)	165.46 (± 27.793)		
Race, Other, n=30,31	179.13 (± 32.374)	150.64 (± 31.914)		

Notes:

[57] - ITT-E Population

[58] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Baseline plasma HIV-1 RNA,<=100000. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, and treatment and HIV-1 RNA interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	19.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.23
upper limit	49.83

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Baseline plasma HIV-1 RNA,>100000. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, and treatment and HIV-1 RNA interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-57.07
upper limit	58.4

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Baseline CD4+ cell count,<=200. Following covariates were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, and treatment and Baseline CD4+ cell count interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	36.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.94
upper limit	129.63

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Baseline CD4+ cell count,>200. Following covariates were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, and treatment and Baseline CD4+ cell count interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	14.37

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.38
upper limit	42.12

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Age<35. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	25.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.56
upper limit	59.85

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Age 35 to <50. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-7.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.98
upper limit	40.34

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Age>=50. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, age, and treatment and age interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	29.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-55.47
upper limit	114.38

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Female. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, gender, and treatment and gender interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	17.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.89
upper limit	85.23

Statistical analysis title	Statistical Analysis 9
Statistical analysis description:	
Male. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, gender, and treatment and gender interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	15.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	44.21

Secondary: Change from Baseline in EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L)

utility score at Weeks 4, 24, 48	
End point title	Change from Baseline in EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L) utility score at Weeks 4, 24, 48

End point description:

EQ-5D-5L questionnaire provides a profile of participant function and a global health state rating. The five-item measure has 1 question assessing each of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression and 5 levels for each dimension including 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems and 5=extreme problems. The health state is defined by combining the levels of answers from each of the 5 questions. Each health state is referred to in terms of a 5 digit code. Health state 5 digit code is translated into utility score, which is valued up to 1 (perfect health) with lower values meaning worse state. EQ-5D-5L utility score ranges from -0.281 to 1. Higher scores indicate better health. Baseline was the latest pre-dose assessment and change from Baseline=post-dose value minus Baseline value. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline and Weeks 4, 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[59]	358[60]		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4, n=349, 348	0.0130 (± 0.00362)	0.0078 (± 0.00353)		
Week 24, n=352, 351	0.0131 (± 0.00371)	0.0168 (± 0.00333)		
Week 48, n=352, 351	0.0134 (± 0.00384)	0.0129 (± 0.00349)		

Notes:

[59] - ITT-E Population

[60] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 4. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count (factor), and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit with visit as the repeated factor

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.302
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.0052
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0047
upper limit	0.0152

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Week24. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count (factor), and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit with visit as the repeated factor	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.45
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.0038
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0136
upper limit	0.006

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Week48. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count (factor), and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit with visit as the repeated factor	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.934
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.0004
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0098
upper limit	0.0106

Secondary: Change from Baseline in EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L) Thermometer Scores at Weeks 4, 24 48

End point title	Change from Baseline in EuroQol – 5 Dimensions – 5 Levels (EQ-5D-5L) Thermometer Scores at Weeks 4, 24 48

End point description:

EQ-5D-5L questionnaire provides a profile of participant function and a global health state rating. The five-item measure has one question assessing each of five dimensions: mobility, self-care, usual

activities, pain/discomfort, and anxiety/depression and 5 levels for each dimension including 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems and 5=extreme problems. EQ-5D-5L included EQ visual Analogue scale (EQ VAS) 'Thermometer' which provided Self-rated current health status. Score ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). MMRM was run on the LOCF dataset, using the observed margins (OM) option. Baseline was the latest pre-dose assessment value and change from Baseline=post-dose value minus Baseline value. Only those participants available at the specified time points were analyzed (represented by n=x in the category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and Weeks 4, 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	356[61]	358[62]		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 4, n=349, 348	2.3 (± 0.48)	1.2 (± 0.52)		
Week 24, n=352, 350	3.7 (± 0.54)	3.2 (± 0.51)		
Week 48, n=352, 350	4.3 (± 0.49)	2.8 (± 0.49)		

Notes:

[61] - ITT-E Population

[62] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 4. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA (factor),Baseline CD4+ cell count (factor), Baseline EQ-5D thermometer, treatment*visit and Baseline EQ-5D thermometer*visit with visit as the repeated factor

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.137
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	2.4

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week24. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA (factor),Baseline CD4+ cell count (factor), Baseline EQ-5D thermometer, treatment*visit and Baseline EQ-5D thermometer*visit with visit

as the repeated factor

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.458
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	2

Statistical analysis title	Statistical Analysis 3

Statistical analysis description:

Week48. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA (factor),Baseline CD4+ cell count (factor), Baseline EQ-5D thermometer, treatment*visit and Baseline EQ-5D thermometer*visit with visit as the repeated factor

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	714
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.031
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	2.8

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Post-Baseline serious adverse events (SAEs) and non-serious adverse events (AEs) were collected from start of the study treatment up to Week 48 (data cut-off for primary analysis).	
Adverse event reporting additional description:	
Post-Baseline SAEs and non-serious AEs were reported for the Safety Population.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of dolutegravir plus tenofovir/emtricitabine (DTG + TDF/FTC) fixed dose combination (FDC) once daily for 48 weeks.	
Reporting group title	DTG + 3TC
Reporting group description:	
Participants received a two-drug regimen of dolutegravir plus lamivudine (DTG + 3TC) once daily for 48 weeks.	

Serious adverse events	DTG + TDF/FTC	DTG + 3TC	
Total subjects affected by serious adverse events			
subjects affected / exposed	22 / 358 (6.15%)	21 / 356 (5.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (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 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (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			
Asthma			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Substance-induced psychotic disorder			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
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			

Head injury			
subjects affected / exposed	1 / 358 (0.28%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Polyneuropathy			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (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			
Lymphadenopathy			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			

subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Rhabdomyolysis			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Hepatitis A			
subjects affected / exposed	4 / 358 (1.12%)	3 / 356 (0.84%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 358 (0.28%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 358 (0.28%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abscess limb			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis C			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chagoma			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter gastritis			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			

subjects affected / exposed	1 / 358 (0.28%)	0 / 356 (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	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	0 / 358 (0.00%)	1 / 356 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	DTG + TDF/FTC	DTG + 3TC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 358 (63.13%)	215 / 356 (60.39%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	11 / 358 (3.07%)	8 / 356 (2.25%)	
occurrences (all)	11	8	
Vascular disorders			
Hypertension			
subjects affected / exposed	7 / 358 (1.96%)	9 / 356 (2.53%)	
occurrences (all)	7	10	
Nervous system disorders			
Headache			
subjects affected / exposed	44 / 358 (12.29%)	40 / 356 (11.24%)	
occurrences (all)	73	58	
Dizziness			
subjects affected / exposed	9 / 358 (2.51%)	8 / 356 (2.25%)	
occurrences (all)	9	10	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	11 / 358 (3.07%)	15 / 356 (4.21%)	
occurrences (all)	12	19	
Fatigue			
subjects affected / exposed	12 / 358 (3.35%)	13 / 356 (3.65%)	
occurrences (all)	13	15	
Influenza like illness			
subjects affected / exposed	12 / 358 (3.35%)	11 / 356 (3.09%)	
occurrences (all)	18	11	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	42 / 358 (11.73%)	33 / 356 (9.27%)	
occurrences (all)	55	42	
Nausea			
subjects affected / exposed	30 / 358 (8.38%)	12 / 356 (3.37%)	
occurrences (all)	33	12	
Abdominal pain			
subjects affected / exposed	9 / 358 (2.51%)	11 / 356 (3.09%)	
occurrences (all)	10	11	
Dyspepsia			
subjects affected / exposed	8 / 358 (2.23%)	7 / 356 (1.97%)	
occurrences (all)	8	10	
Haemorrhoids			
subjects affected / exposed	7 / 358 (1.96%)	8 / 356 (2.25%)	
occurrences (all)	7	8	
Abdominal pain upper			
subjects affected / exposed	8 / 358 (2.23%)	4 / 356 (1.12%)	
occurrences (all)	10	6	
Vomiting			
subjects affected / exposed	4 / 358 (1.12%)	8 / 356 (2.25%)	
occurrences (all)	5	9	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 358 (3.91%)	7 / 356 (1.97%)	
occurrences (all)	14	7	
Oropharyngeal pain			

subjects affected / exposed	12 / 358 (3.35%)	7 / 356 (1.97%)	
occurrences (all)	12	7	
Rhinitis allergic			
subjects affected / exposed	3 / 358 (0.84%)	9 / 356 (2.53%)	
occurrences (all)	3	14	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	29 / 358 (8.10%)	16 / 356 (4.49%)	
occurrences (all)	32	17	
Depression			
subjects affected / exposed	10 / 358 (2.79%)	9 / 356 (2.53%)	
occurrences (all)	10	9	
Anxiety			
subjects affected / exposed	6 / 358 (1.68%)	8 / 356 (2.25%)	
occurrences (all)	7	8	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	19 / 358 (5.31%)	19 / 356 (5.34%)	
occurrences (all)	20	25	
Arthralgia			
subjects affected / exposed	11 / 358 (3.07%)	5 / 356 (1.40%)	
occurrences (all)	12	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	37 / 358 (10.34%)	33 / 356 (9.27%)	
occurrences (all)	50	45	
Upper respiratory tract infection			
subjects affected / exposed	22 / 358 (6.15%)	24 / 356 (6.74%)	
occurrences (all)	27	26	
Pharyngitis			
subjects affected / exposed	13 / 358 (3.63%)	23 / 356 (6.46%)	
occurrences (all)	18	25	
Syphilis			
subjects affected / exposed	15 / 358 (4.19%)	17 / 356 (4.78%)	
occurrences (all)	15	18	
Bronchitis			

subjects affected / exposed	11 / 358 (3.07%)	20 / 356 (5.62%)	
occurrences (all)	12	21	
Influenza			
subjects affected / exposed	11 / 358 (3.07%)	14 / 356 (3.93%)	
occurrences (all)	13	16	
Sinusitis			
subjects affected / exposed	9 / 358 (2.51%)	12 / 356 (3.37%)	
occurrences (all)	10	14	
Gastroenteritis			
subjects affected / exposed	10 / 358 (2.79%)	10 / 356 (2.81%)	
occurrences (all)	10	10	
Gonorrhoea			
subjects affected / exposed	10 / 358 (2.79%)	9 / 356 (2.53%)	
occurrences (all)	13	12	
Tonsillitis			
subjects affected / exposed	8 / 358 (2.23%)	10 / 356 (2.81%)	
occurrences (all)	8	11	
Herpes zoster			
subjects affected / exposed	12 / 358 (3.35%)	4 / 356 (1.12%)	
occurrences (all)	12	4	
Pharyngotonsillitis			
subjects affected / exposed	8 / 358 (2.23%)	6 / 356 (1.69%)	
occurrences (all)	11	6	
Respiratory tract infection			
subjects affected / exposed	9 / 358 (2.51%)	5 / 356 (1.40%)	
occurrences (all)	12	8	
Respiratory tract infection viral			
subjects affected / exposed	8 / 358 (2.23%)	5 / 356 (1.40%)	
occurrences (all)	9	6	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	4 / 358 (1.12%)	9 / 356 (2.53%)	
occurrences (all)	4	9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2017	Amendment No. 1: The double barrier method of contraception (male condom combined with a vaginal spermicide) was added in this study as a permitted method for preventing pregnancy in females of reproductive potential. Exclusion criterion #15 (limitations on investigational drug use) was broadened to include additional countries as needed. Inclusion of Portugal was required by the Portuguese National Ethics Committee for Clinical Research. Assessment of weight at Weeks 96 and 144 was added to monitor the incidence of significant weight gain with dolutegravir use. Assessment of inflammation biomarkers (IL-6, hs-CRP) at Day 1, and Weeks 48, 96 and 144, was added as a new exploratory endpoint. Assessment of telomere length at Day 1, and Weeks 96 and 144, was added as a new exploratory endpoint. For clarification purposes, the 'peripheral blood mononuclear cell (PBMC)' sample in Time and Events table and HIV-1 Exploratory Analyses was renamed as a 'whole blood' sample. The Day 1 'PBMC' sample (now named 'whole blood' sample) originally designated for virology use was additionally designated for telomere length measurement, where possible. Additional whole blood samples were added for measurement of telomere length at Week 96 and Week 144. A description of commercial image dolutegravir tablets was added to Investigational Product and Other Study Treatment to allow use of commercial material as well as clinical trial material during the study. The physical description for open-label lamivudine was corrected. Standard procedures for forwarding pregnancy information to the Antiretroviral Pregnancy Register were added. For clarification purposes, the AE severity gradings in were updated to be consistent. This change has no impact on the investigator's evaluation of adverse events. Minor revisions were made to the text to provide updated information, correct errors and improve accuracy and consistency.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported