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	2016-000459-28
Trial protocol	DE BE PT ES FR IT
Global end of trial date	

Results information

Result version number	v1
This version publication date	13 April 2019
First version publication date	13 April 2019

Trial information

Trial identification

Sponsor protocol code	205543

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, GSKClinicalSupportHD@gsk.com
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	04 April 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 participants

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 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: 77
Country: Number of subjects enrolled	Australia: 14
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Italy: 52
Country: Number of subjects enrolled	Mexico: 43
Country: Number of subjects enrolled	Peru: 23
Country: Number of subjects enrolled	Poland: 9
Country: Number of subjects enrolled	Portugal: 20
Country: Number of subjects enrolled	Romania: 21
Country: Number of subjects enrolled	Russian Federation: 87
Country: Number of subjects enrolled	Spain: 98
Country: Number of subjects enrolled	Switzerland: 13
Country: Number of subjects enrolled	Taiwan: 55
Country: Number of subjects enrolled	United States: 135
Country: Number of subjects enrolled	United Kingdom: 28
Worldwide total number of subjects	722
EEA total number of subjects	262

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)	719
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study is a Phase 3, randomized, double-blind, parallel group, non-inferiority study. A total of 104 investigational centers in 18 countries randomized one or more participants in this multicenter study. The results presented are based on the primary analysis at Week 48.

Pre-assignment

Screening details:

Total of 722 participants were enrolled and randomized; however only 719 participants (3 participants were never dosed following randomization as they withdrew consent to participate in study) were dosed in to the study to receive either dolutegravir plus lamivudine (DTG+3TC) or dolutegravir plus tenofovir/emtricitabine (DTG+TDF/FTC).

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	Subject, Investigator, Monitor

Arms

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

Arm description:

Participants received a two-drug regimen of DTG + 3TC administered orally, once daily for 48 weeks.

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

Dosage and administration details:

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:

3TC 300 mg capsule, oral administration, once daily.

Arm title	DTG + TDF/FTC

Arm description:

Participants received a three-drug regimen of DTG + TDF/FTC FDC administered orally, once daily for 48 weeks.

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

Dosage and administration details: DTG 50 mg tablet, oral administration, once daily.	
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: 300 mg TDF/ 200 mg FTC capsule, oral administration, once daily.	

Number of subjects in period 1[1]	DTG + 3TC	DTG + TDF/FTC
Started	360	359
Completed	0	0
Not completed	360	359
Adverse event, serious fatal	2	-
Consent withdrawn by subject	7	6
Physician decision	2	2
Adverse event, non-fatal	6	5
Protocol specific withdrawal criteria	-	2
Ongoing at the time of the analysis	330	335
Lost to follow-up	6	5
Lack of efficacy	2	2
Protocol deviation	5	2

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 722 participants were enrolled and randomized however only 719 participants (3 participants were never dosed following randomization as they withdrew consent to participate in study) were dosed in to the study to receive either dolutegravir plus lamivudine (DTG+3TC) or dolutegravir plus tenofovir/emtricitabine (DTG+TDF/FTC).

Baseline characteristics

Reporting groups	
Reporting group title	DTG + 3TC
Reporting group description:	
Participants received a two-drug regimen of DTG + 3TC administered orally, once daily for 48 weeks.	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of DTG + TDF/FTC FDC administered orally, once daily for 48 weeks.	

Reporting group values	DTG + 3TC	DTG + TDF/FTC	Total
Number of subjects	360	359	719
Age categorical Units: Subjects			
Overall number of baseline subjects	360	359	719
Age Continuous Units: Years			
arithmetic mean	34.6	34.4	
standard deviation	± 10.72	± 10.35	-
Sex: Female, Male Units: Subjects			
Female	54	46	100
Male	306	313	619
Race/Ethnicity, Customized Units: Subjects			
American (Am) Indian or Alaska (Al.) native	21	24	45
Asian-Central/South Asian heritage (H.)	0	3	3
Asian - East Asian H.	28	26	54
Asian - South East Asian H.	6	1	7
Black or African Am	55	40	95
Native Hawaiian or other Pacific Islander	0	5	5
White (Wt)-Arabic/North African H.	3	3	6
Wt-Wt/Caucasian (Ca.)/European (Eu.) H.	234	246	480
Am Indian or Al. native and Wt	12	10	22
Black or African Am and Wt	1	1	2

End points

End points reporting groups

Reporting group title	DTG + 3TC
Reporting group description:	
Participants received a two-drug regimen of DTG + 3TC administered orally, once daily for 48 weeks.	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of DTG + TDF/FTC FDC administered orally, 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 invetigational 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	360[1]	359[2]		
Units: Percentage of participants				
number (confidence interval 95%)	93 (90.4 to 95.7)	94 (91.4 to 96.4)		

Notes:

[1] - ITT-E Population

[2] - ITT-E Population

Statistical analyses

Statistical analysis title	Stat 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 copies per milliliter) and CD4+ cell count (<= vs. >200 cells per cubic millimeter [cells/mm^3].	
Comparison groups	DTG + TDF/FTC v DTG + 3TC

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Adjusted difference in proportion
Point estimate	-0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	2.9

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 was greater than -10%.

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

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL at Weeks 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 CMH 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	360[4]	359[5]		
Units: Percentage of participants				
number (confidence interval 95%)	94 (91.4 to 96.4)	94 (91.4 to 96.4)		

Notes:

[4] - ITT-E Population

[5] - ITT-E Population

Statistical analyses

Statistical analysis title	Stat 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 copies per milliliter) and CD4+ cell count (<= vs. >200 cells/mm^3).

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted difference in proportion
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.6

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 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	360[6]	359[7]		
Units: Days				
median (inter-quartile range (Q1-Q3))	29.0 (29.0 to 55.0)	29.0 (29.0 to 57.0)		

Notes:

[6] - ITT-E Population

[7] - ITT-E Population

Statistical analyses

Statistical analysis title	Stat 1

Statistical analysis description:

Hazard ratios were estimated using the Cox proportional hazard regression model.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.825 [8]
Method	Generalised Wilcoxon procedure
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	1.18

Notes:

[8] - The generalised 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+ cells. Analysis was performed 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	360[9]	359[10]		
Units: Cells/mm^3				
arithmetic mean (standard deviation)				
Week 24, n=349,345	650.4 (± 257.02)	633.0 (± 287.37)		
Week 48, n=337,340	688.1 (± 266.39)	689.8 (± 308.49)		

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+ cells. Analysis was performed by flow cytometry. Baseline value is defined as the the latest pre-dose assessment. Change from Baseline was defined as value at the indicated time point minus Baseline value. Adjusted least 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 and Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360[11]	359[12]		
Units: Cells/mm^3				
least squares mean (standard error)				
Week 24, n=349, 345	188.8 (± 8.77)	163.2 (± 9.08)		
Week 48, n=337, 340	225.7 (± 8.94)	217.2 (± 9.93)		

Notes:

[11] - ITT-E Population

[12] - ITT-E Population

Statistical analyses

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.043
Method	Mixed Model Repeated Measures (MMRM)
Parameter estimate	Mean difference (net)
Point estimate	25.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	50.4

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.523
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	8.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.7
upper limit	34.8

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 progressions 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 enrollment 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 enrollment 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	360[13]	359[14]		
Units: Participants				
No disease progression	356	358		
From CDC Stage 1 to CDC Stage 3 Event	0	0		
From CDC Stage 2 to CDC Stage 3 Event	1	1		
From CDC Stage 3 to New CDC Stage 3 Event	1	0		
From CDC Stage 1, 2 or 3 to Death	2	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 genotypic 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.

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	2[15]	2[16]		
Units: Participants				
INSTI Mutations	0	0		
Major mutations of the 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 were interpreted through a proprietary algorithm (from Monogram Biosciences) and provides the overall susceptibility of the drugs (Abacavir [ABC], elvitegravir [EGV], raltegravir [RAL], zidovudine [AZT], stavudine [D4T], didanosine [DDI]), emtricitabine [FTC], tenofovir disiproxil fumarate [TDF]). Partially sensitive and resistant cells 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	2[17]	2[18]		
Units: Participants				
INSTI, DTG, Sensitive, n=2,1	2	1		
INSTI, DTG, Resistant, n=2,1	0	0		
INSTI, EVG, Sensitive, n=2,1	2	1		
INSTI, EVG, Resistant, n=2,1	0	0		
INSTI, RAL, Sensitive, n=2,1	2	1		
INSTI, RAL, Resistant, n=2,1	0	0		
NRTI, 3TC, Sensitive, n=2,2	2	2		
NRTI, 3TC, Resistant, n=2,2	0	0		
NRTI, ABC, Sensitive, n=2,2	2	2		

NRTI, ABC, Resistant, n=2,2	0	0		
NRTI, AZT, Sensitive, n=2,2	2	2		
NRTI, AZT, Resistant, n=2,2	0	0		
NRTI, D4T, Sensitive, n=2,2	2	2		
NRTI, D4T, Resistant, n=2,2	0	0		
NRTI, DDI, Sensitive, n=2,2	2	2		
NRTI, DDI, Resistant, n=2,2	0	0		
NRTI, FTC, Sensitive, n=2,2	2	2		
NRTI, FTC, Resistant, n=2,2	0	0		
NRTI, TDF, Sensitive, n=2,2	2	2		
NRTI, TDF, Resistant, n=2,2	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 Analyses presented herein used a data cut-off date of 22 May 2018 (for Week 48 database freeze), i.e. may include data collected after a participant's Week 48 visit..

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	360[19]	359[20]		
Units: Participants				
Any AE	267	284		
Any SAE	29	33		

Notes:

[19] - Safety Population

[20] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs by maximum severity grades

End point title	Number of participants with AEs by maximum 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. Analyses presented herein used a data cut-off date of 22 May 2018 (for Week 48 database freeze), i.e. may include data collected after a participant's Week 48 visit.

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	360[21]	359[22]		
Units: Participants				
Grade 1 AEs	79	93		
Grade 2 AEs	161	159		
Grade 3 AEs	19	29		
Grade 4 AEs	6	3		
Grade 5 AEs	2	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 by maximum grade have been presented. Analyses presented herein used a data cut-off date of 22 May 2018 (for Week 48 database freeze), i.e. may include data collected after a participant's Week 48 visit.

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	360[23]	359[24]		
Units: Participants				
Any drug related AE	55	75		
Drug related AEs with maximum toxicity Grade 1	34	53		
Drug related AEs with maximum toxicity Grade 2	17	17		
Drug related AEs with maximum toxicity Grade 3	3	4		
Drug related AEs with maximum toxicity Grade 4	1	1		
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 platelet count, neutrophils, hemoglobin, and Leukocytes. Any abnormality was graded according to DAIDS toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). Only those participants with maximum post-Baseline emergent hematology toxicities in any of the listed 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	360[25]	359[26]		
Units: Participants				
Hemoglobin, Grades 1 to 4	8	7		
Hemoglobin, Grades 2 to 4	5	4		
Hemoglobin, Grades 3 to 4	2	1		
Hemoglobin, Grade 1	3	3		
Hemoglobin, Grade 2	3	3		
Hemoglobin, Grade 3	1	1		
Hemoglobin, Grade 4	1	0		
Leukocytes, Grades 1 to 4	4	3		
Leukocytes, Grades 2 to 4	1	0		
Leukocytes, Grades 3 to 4	0	0		

Leukocytes, Grade 1	3	3		
Leukocytes, Grade 2	1	0		
Leukocytes, Grade 3	0	0		
Leukocytes, Grade 4	0	0		
Neutrophils, Grades 1 to 4	14	6		
Neutrophils, Grades 2 to 4	4	2		
Neutrophils, Grades 3 to 4	1	1		
Neutrophils, Grade 1	10	4		
Neutrophils, Grade 2	3	1		
Neutrophils, Grade 3	1	1		
Neutrophils, Grade 4	0	0		
Platelets, Grades 1 to 4	11	9		
Platelets, Grades 2 to 4	5	5		
Platelets, Grades 3 to 4	0	0		
Platelets, Grade 1	6	4		
Platelets, Grade 2	5	5		
Platelets, Grade 3	0	0		
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), Albumin, Alkaline Phosphatase (ALP), Bilirubin, Carbon dioxide (CO2), Cholesterol, Creatine kinase (CPK), Creatinine, Direct Bilirubin, Glomerular filtration rate (GFR), Hypercalcemia, Hyperglycemia, Hyperkalemia, Hypernatremia, Hypocalcemia, Hypoglycemia, Hypokalemia and Hyponatremia, Low density lipid (LDL) Cholesterol, Lactate Dehydrogenase, Lipase and Phosphate. Any abnormality was graded according to DAIDS toxicity scales from Grade 1 to 4 (1=Mild, 2=Moderate, 3=Severe, 4=Potentially life threatening). 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	360[27]	359[28]		
Units: Participants				
ALT, Grades 1 to 4	43	51		
ALT, Grades 2 to 4	17	22		
ALT, Grades 3 to 4	9	10		

ALT, Grade 1	26	29		
ALT, Grade 2	8	12		
ALT, Grade 3	4	4		
ALT, Grade 4	5	6		
Albumin, Grades 1 to 4	0	1		
Albumin, Grades 2 to 4	0	1		
Albumin, Grades 3 to 4	0	1		
Albumin, Grade 1	0	0		
Albumin, Grade 2	0	0		
Albumin, Grade 3	0	1		
Albumin, Grade 4	0	0		
ALP, Grades 1 to 4	6	14		
ALP, Grades 2 to 4	2	3		
ALP, Grades 3 to 4	0	1		
ALP, Grade 1	4	11		
ALP, Grade 2	2	2		
ALP, Grade 3	0	1		
ALP, Grade 4	0	0		
AST, Grades 1 to 4	42	56		
AST, Grades 2 to 4	17	23		
AST, Grades 3 to 4	7	12		
AST, Grade 1	25	33		
AST, Grade 2	10	11		
AST, Grade 3	3	9		
AST, Grade 4	4	3		
Bilirubin, Grades 1 to 4	33	38		
Bilirubin, Grades 2 to 4	8	11		
Bilirubin, Grades 3 to 4	3	3		
Bilirubin, Grade 1	25	27		
Bilirubin, Grade 2	5	8		
Bilirubin, Grade 3	0	2		
Bilirubin, Grade 4	3	1		
CO2, Grades 1 to 4	71	87		
CO2, Grades 2 to 4	6	2		
CO2, Grades 3 to 4	0	0		
CO2, Grade 1	65	85		
CO2, Grade 2	6	2		
CO2, Grade 3	0	0		
CO2, Grade 4	0	0		
Cholesterol, Grades 1 to 4	70	26		
Cholesterol, Grades 2 to 4	11	5		
Cholesterol, Grades 3 to 4	0	0		
Cholesterol, Grade 1	59	21		
Cholesterol, Grade 2	11	5		
Cholesterol, Grade 3	0	0		
Cholesterol, Grade 4	0	0		
CK, Grades 1 to 4	61	48		
CK, Grades 2 to 4	34	28		
CK, Grades 3 to 4	19	17		
CK, Grade 1	27	20		
CK, Grade 2	15	11		
CK, Grade 3	9	6		

CK, Grade 4	10	11		
Creatinine, Grades 1 to 4	14	19		
Creatinine, Grades 2 to 4	3	2		
Creatinine, Grades 3 to 4	0	1		
Creatinine, Grade 1	11	17		
Creatinine, Grade 2	3	1		
Creatinine, Grade 3	0	1		
Creatinine, Grade 4	0	0		
Direct Bilirubin, Grades 1 to 4	7	7		
Direct Bilirubin, Grades 2 to 4	7	7		
Direct Bilirubin, Grades 3 to 4	7	7		
Direct Bilirubin, Grade 1	0	0		
Direct Bilirubin, Grade 2	0	0		
Direct Bilirubin, Grade 3	7	7		
Direct Bilirubin, Grade 4	0	0		
GFR, Grades 1 to 4	154	190		
GFR, Grades 2 to 4	154	190		
GFR, Grades 3 to 4	13	18		
GFR, Grade 1	0	0		
GFR, Grade 2	141	172		
GFR, Grade 3	13	17		
GFR, Grade 4	0	1		
Hypercalcaemia, Grades 1 to 4	3	5		
Hypercalcaemia, Grades 2 to 4	0	1		
Hypercalcaemia, Grades 3 to 4	0	1		
Hypercalcemia, Grade 1	3	4		
Hypercalcaemia, Grade 2	0	0		
Hypercalcaemia, Grade 3	0	0		
Hypercalcaemia, Grade 4	0	1		
Hyperglycaemia, Grades 1 to 4	74	57		
Hyperglycaemia, Grades 2 to 4	30	21		
Hyperglycaemia, Grades 3 to 4	2	3		
Hyperglycaemia, Grade 1	44	36		
Hyperglycaemia, Grade 2	28	18		
Hyperglycaemia, Grade 3	2	2		
Hyperglycaemia, Grade 4	0	1		
Hyperkalemia, Grades 1 to 4	4	4		
Hyperkalemia, Grades 2 to 4	1	0		
Hyperkalemia, Grades 3 to 4	0	0		
Hyperkalemia, Grade 1	3	4		
Hyperkalemia, Grade 2	1	0		
Hyperkalemia, Grade 3	0	0		
Hyperkalemia, Grade 4	0	0		
Hypernatremia, Grades 1 to 4	1	5		
Hypernatremia, Grades 2 to 4	0	0		
Hypernatremia, Grades 3 to 4	0	0		
Hypernatremia, Grade 1	1	5		
Hypernatremia, Grade 2	0	0		
Hypernatremia, Grade 3	0	0		
Hypernatremia, Grade 4	0	0		
Hypocalcaemia, Grades 1 to 4	7	10		
Hypocalcaemia, Grades 2 to 4	1	5		

Hypocalcaemia, Grades 3 to 4	0	1		
Hypocalcaemia, Grade 1	6	5		
Hypocalcaemia, Grade 2	1	4		
Hypocalcaemia, Grade 3	0	1		
Hypocalcaemia, Grade 4	0	0		
Hypoglycaemia, Grades 1 to 4	13	13		
Hypoglycaemia, Grades 2 to 4	4	4		
Hypoglycaemia, Grades 3 to 4	3	1		
Hypoglycaemia, Grade 1	9	9		
Hypoglycaemia, Grade 2	1	3		
Hypoglycaemia, Grade 3	2	0		
Hypoglycaemia, Grade 4	1	1		
Hypokalemia, Grades 1 to 4	3	0		
Hypokalemia, Grades 2 to 4	0	0		
Hypokalemia, Grades 3 to 4	0	0		
Hypokalemia, Grade 1	3	0		
Hypokalemia, Grade 2	0	0		
Hypokalemia, Grade 3	0	0		
Hypokalemia, Grade 4	0	0		
Hyponatremia, Grades 1 to 4	14	18		
Hyponatremia, Grades 2 to 4	0	2		
Hyponatremia, Grades 3 to 4	0	0		
Hyponatremia, Grade 1	14	16		
Hyponatremia, Grade 2	0	2		
Hyponatremia, Grade 3	0	0		
Hyponatremia, Grade 4	0	0		
LDL Cholesterol, Grades 1 to 4	48	22		
LDL Cholesterol, Grades 2 to 4	14	5		
LDL Cholesterol, Grades 3 to 4	3	0		
LDL Cholesterol, Grade 1	34	17		
LDL Cholesterol, Grade 2	11	5		
LDL Cholesterol, Grade 3	3	0		
LDL Cholesterol, Grade 4	0	0		
Lactate Dehydrogenase, Grades 1 to 4	3	2		
Lactate Dehydrogenase, Grades 2 to 4	3	0		
Lactate Dehydrogenase, Grades 3 to 4	0	0		
Lactate Dehydrogenase, Grade 1	0	2		
Lactate Dehydrogenase, Grade 2	3	0		
Lactate Dehydrogenase, Grade 3	0	0		
Lactate Dehydrogenase, Grade 4	0	0		
Lipase, Grades 1 to 4	48	60		
Lipase, Grades 2 to 4	21	28		
Lipase, Grades 3 to 4	2	10		
Lipase, Grade 1	27	32		
Lipase, Grade 2	19	18		
Lipase, Grade 3	0	9		
Lipase, Grade 4	2	1		
Phosphate, Grades 1 to 4	53	51		
Phosphate, Grades 2 to 4	31	33		
Phosphate, Grades 3 to 4	2	4		
Phosphate, Grade 1	22	18		
Phosphate, Grade 2	29	29		

Phosphate, Grade 3	2	4		
Phosphate, Grade 4	0	0		
Triglycerides, Grades 1 to 4	58	52		
Triglycerides, Grades 2 to 4	11	7		
Triglycerides, Grades 3 to 4	3	1		
Triglycerides, Grade 1	47	45		
Triglycerides, Grade 2	8	6		
Triglycerides, Grade 3	3	1		
Triglycerides, Grade 4	0	0		

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. Number of participants who discontinued treatment due to AEs have been reported. Analyses presented herein used a data cut-off date of 19 January 2018 and 22 May 2018, respectively, for the Week 24 database freeze and Week 48 database freeze), i.e. may include data collected after a participant's Week 24 or 48 visit, respectively.

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	360[29]	359[30]		
Units: Participants				
Up to Week 24	6	4		
Up to Week 48	8	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 samples were collected to perform evaluation of renal inflammation biomarkers which included Serum Cystatin C and Serum Retinol Binding Protein (RBP). Baseline value is the the latest pre-dose assessment. Change from Baseline was defined as value at indicated time point minus Baseline value. Biomarkers were adjusted for treatment, visit, Baseline plasma HIV-1 RNA, baseline CD4+ cell count, age, sex, race, presence of diabetes mellitus, presence of hypertension, 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	360[31]	359[32]		
Units: Milligrams per Liter (mg/L)				
least squares mean (standard error)				
Serum Cystatin C, Week 24, n=345,345	-0.04 (± 0.005)	0.00 (± 0.005)		
Serum Cystatin C, Week 48, n=335,336	-0.05 (± 0.005)	-0.04 (± 0.006)		
Serum RBP, Week 24, n=345,343	1.2 (± 0.42)	1.4 (± 0.48)		
Serum RBP, Week 48, n=334, 334	0.6 (± 0.45)	-0.1 (± 0.42)		

Notes:

[31] - Safety Population

[32] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1

Statistical analysis description:

Week 24. Serum Cystatin C.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.02

Statistical analysis title	Stat 2

Statistical analysis description: Week 48. Serum Cystatin C.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.022
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Statistical analysis title	Stat 3
Statistical analysis description: Week 24. Serum RBP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.797
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.1

Statistical analysis title	Stat 4
Statistical analysis description: Week 48. Serum RBP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.258
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	1.9

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 samples were collected to perform evaluation of renal inflammation biomarkers which included Serum GFR from cystatin C adjusted using CKD-EPI (GFR-cystatin C adjusted) and Serum or Plasma GFR from creatinine adjusted using CKD-EPI. Baseline value is the latest pre-dose Assessment. Change from Baseline was defined as value at the indicated time point minus Baseline value. Biomarkers were adjusted for treatment, visit, Baseline plasma HIV-1 RNA, baseline CD4+ cell count, age, sex, race, presence of diabetes mellitus, presence of hypertension, 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	360[33]	359[34]		
Units: Milliliter/minute/1.73 meter^2				
arithmetic mean (standard error)				
GFR Cystatin C adjusted, Week 24, n=345,345	3.8 (± 0.66)	0.2 (± 0.65)		
GFR Cystatin C adjusted, Week 48, n=335,336	5.4 (± 0.64)	3.6 (± 0.64)		
GFR creatinine adjusted, Week 24, n=346,344	-12.0 (± 0.64)	-15.4 (± 0.59)		
GFR creatinine adjusted, Week 48, n=335, 337	-12.1 (± 0.60)	-15.4 (± 0.61)		

Notes:

[33] - Safety Population

[34] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1

Statistical analysis description:

Week 24. GFR Cystatin C adjusted.

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.8
upper limit	5.4

Statistical analysis title	Stat 2
Statistical analysis description: Week 48. GFR Cystatin C adjusted.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.056
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	3.5

Statistical analysis title	Stat 3
Statistical analysis description: Week 24. GFR creatinine adjusted	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	3.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.7
upper limit	5.2

Statistical analysis title	Stat 4
Statistical analysis description: Week 48. GFR creatinine adjusted.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.6
upper limit	5

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 samples were collected to perform evaluation of renal inflammation biomarker which included Serum or Plasma Creatinine. Baseline value is defined as the the latest pre-dose assessment. Change from Baseline was calculated as value at the inidcated time point minus Baseline value. Biomarkers were adjusted for treatment, visit, Baseline plasma HIV-1 RNA, baseline CD4+ cell count, age, sex, race, presence of diabetes mellitus, presence of hypertension, 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	360[35]	359[36]		
Units: Micromoles per Liter (umol/L)				
arithmetic mean (standard deviation)				
Serum or Plasma Creatinine, Week 24, n=346, 344	10.51 (± 0.548)	13.53 (± 0.507)		
Serum or Plasma Creatinine, Week 48, n=335, 337	10.32 (± 0.519)	13.44 (± 0.540)		

Notes:
[35] - Safety Population
[36] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1
Statistical analysis description: Week 24. Serum Plasma Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.49
upper limit	-1.55

Statistical analysis title	Stat 2
Statistical analysis description: Week 48. Serum Plasma creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-3.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.59
upper limit	-1.65

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: 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 was the latest pre-dose assessment. Change from Baseline was performed on log-transformed data. Ratio to Baseline was calculated as ratio of post-dose visit value over Baseline value. Geometric mean ratio and 95% CI of geometric mean ratio have been presented. Biomarkers were Adjusted for treatment, Baseline plasma HIV-1 RNA, Baseline CD4+ cell count, age, sex, race, presence of diabetes mellitus, presence of hypertension, loge transformed Baseline biomarker value, treatment and visit interaction, and loge transformed 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 Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360[37]	359[38]		
Units: Ratio				
geometric mean (confidence interval 95%)				
Serum B2M, Week 24, n=344,346	0.809 (0.794 to 0.824)	0.882 (0.867 to 0.898)		
Serum B2M, Week 48, n=335,336	0.811 (0.796 to 0.827)	0.887 (0.871 to 0.904)		
Urine B2M, Week 24, n=124,106	0.844 (0.755 to 0.944)	1.129 (0.974 to 1.309)		
Urine B2M, Week 48, n=109, 103	0.917 (0.804 to 1.046)	1.323 (1.066 to 1.642)		
Urine Albumin/Creatinine, Week 24, n=259, 251	0.907 (0.844 to 0.976)	1.021 (0.940 to 1.109)		
Urine Albumin/Creatinine , Week 48, n=249, 240	0.911 (0.835 to 0.994)	0.971 (0.891 to 1.058)		
Urine B2M/Urine Creatinine , Week 24, n=122, 104	0.880 (0.779 to 0.993)	1.126 (0.988 to 1.282)		
Urine B2M/Urine Creatinine , Week 48, n=108, 103	0.969 (0.854 to 1.099)	1.307 (1.077 to 1.586)		
Urine Phosphate, Week 24, n=343, 340	1.041 (0.955 to 1.134)	1.063 (0.978 to 1.157)		
Urine Phosphate , Week 48, n=335, 332	1.121 (1.031 to 1.220)	1.056 (0.974 to 1.144)		
Urine Protein/Creatinine , Week 24, n=263,279	0.818 (0.779 to 0.859)	0.991 (0.941 to 1.043)		
Urine Protein/Creatinine , Week 48, n=259, 261	0.866 (0.818 to 0.917)	1.007 (0.954 to 1.062)		
Urine RBP 4, Week 24, n=340, 338	0.656 (0.591 to 0.729)	0.824 (0.738 to 0.921)		
Urine RBP 4, Week 48, n=333, 331	0.740 (0.666 to 0.822)	0.819 (0.730 to 0.919)		
Urine RBP 4/Urine Creatinine , Week 24, n=338, 335	0.670 (0.614 to 0.730)	0.811 (0.741 to 0.888)		

Urine RBP 4/Urine Creatinine , Week 48, n=331, 328	0.749 (0.689 to 0.814)	0.844 (0.774 to 0.920)		

Notes:

[37] - Safety Population

[38] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1
Statistical analysis description: Week 24. Serum B2M.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.917
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.893
upper limit	0.941

Statistical analysis title	Stat 2
Statistical analysis description: Week 48. Serum B2M.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.914
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	0.939

Statistical analysis title	Stat 3
Statistical analysis description: Week 24. Urine B2M.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.002
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.748
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.621
upper limit	0.901

Statistical analysis title	Stat 4
Statistical analysis description: Week 48. Urine B2M.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.005
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.693
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.538
upper limit	0.892

Statistical analysis title	Stat 5
Statistical analysis description: Week 24. Urine Albumin/Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.036
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.889
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.796
upper limit	0.992

Statistical analysis title	Stat 6
Statistical analysis description: Week 48. Urine Albumin/Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.308
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.938
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.061

Statistical analysis title	Stat 7
Statistical analysis description: Week 24. Urine B2M/Urine Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.007
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.781
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.654
upper limit	0.934

Statistical analysis title	Stat 8
Statistical analysis description: Week 48. Urine B2M/Urine Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.012
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.742
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.588
upper limit	0.935

Statistical analysis title	Stat 9
Statistical analysis description: Week 24. Urine Phosphate.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.728
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.979
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.868
upper limit	1.104

Statistical analysis title	Stat 10
Statistical analysis description: Week 48. Urine Phosphate.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.311
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	1.062
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.945
upper limit	1.194

Statistical analysis title	Stat 11
Statistical analysis description: Week 24. Urine Protein/Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.826
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.769
upper limit	0.887

Statistical analysis title	Stat 12
Statistical analysis description: Week 48. Urine Protein/Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.795
upper limit	0.93

Statistical analysis title	Stat 13
Statistical analysis description: Week 24. Urine RBP 4.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.796
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.683
upper limit	0.927

Statistical analysis title	Stat 14
Statistical analysis description: Week 48. Urine RBP 4.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.2
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.903
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.773
upper limit	1.056

Statistical analysis title	Stat 15
Statistical analysis description: Week 24. Urine RBP/Urine Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.003
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.826
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.728
upper limit	0.936

Statistical analysis title	Stat 16
Statistical analysis description:	
Week 48. Urine RBP/Urine Creatinine.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.052
Method	MMRM
Parameter estimate	Ratio of geometric means
Point estimate	0.888
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.787
upper limit	1.001

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. 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. Baseline value is defined as the latest pre-dose assessment. Change from Baseline was calculated as value at the indicated time point 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 at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360[39]	359[40]		
Units: Micrograms per Liter (ug/L)				
arithmetic mean (standard error)				
Bone-ALP, Week 24, n=345, 346	0.72 (± 0.171)	3.38 (± 0.244)		

Bone-ALP, Week 48, n=334, 337	1.24 (± 0.198)	4.33 (± 0.268)		
Serum Osteocalcin, Week 24, n=345, 346	2.13 (± 0.321)	6.80 (± 0.368)		
Serum Osteocalcin, Week 48, n=335, 336	0.40 (± 0.326)	6.30 (± 0.384)		
PINP, Week 24, n=344, 346	1.7 (± 0.95)	15.2 (± 1.12)		
PINP, Week 48, n=335, 337	0.4 (± 0.79)	13.3 (± 1.06)		
CTX-1, Week 24, n=342, 342	0.1541 (± 0.01247)	0.2812 (± 0.01406)		
CTX-1, Week 48, n=332, 333	0.1345 (± 0.01496)	0.3388 (± 0.01983)		

Notes:

[39] - Safety Population

[40] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1
Statistical analysis description: Week 24, Bone ALP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-2.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.25
upper limit	-2.08

Statistical analysis title	Stat 2
Statistical analysis description: Week 48, Bone ALP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-3.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.75
upper limit	-2.44

Statistical analysis title	Stat 3
Statistical analysis description: Week 28, Serum Osteocalcin.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-4.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.63
upper limit	-3.71

Statistical analysis title	Stat 4
Statistical analysis description: Week 48, Serum Osteocalcin.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.89
upper limit	-4.91

Statistical analysis title	Stat 5
Statistical analysis description: Week 24, Serum PINP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-13.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	-10.6

Statistical analysis title	Stat 6
Statistical analysis description: Week 48, Serum PINP.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	-10.2

Statistical analysis title	Stat 7
Statistical analysis description: Week 24, CTX-1	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.127
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.164
upper limit	-0.09

Statistical analysis title	Stat 8
Statistical analysis description: Week 48, CTX-1.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.2043
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2532
upper limit	-0.1554

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. 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. Baseline value is defined as the latest pre-dose assessment. Change from Baseline was calculated as value at the indicated time point minus Baseline value.

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	360[41]	359[42]		
Units: Nanomoles per Liter (nmol/L)				
least squares mean (standard error)				
Serum Vitamin D, Week 24, n=346, 344	11.2 (± 1.08)	15.4 (± 1.33)		
Serum Vitamin D, Week 48, n=336, 335	0.3 (± 0.92)	0.4 (± 1.01)		

Notes:

[41] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1
Statistical analysis description: Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.015
Method	MMRM
Parameter estimate	Median difference (net)
Point estimate	-4.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.5
upper limit	-0.8

Statistical analysis title	Stat 2
Statistical analysis description: Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.96
Method	MMRM
Parameter estimate	Median difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.8
upper limit	2.6

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 and at Weeks 24, 48

End point values	DTG + 3TC	DTG + TDF/FTC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	360[43]	359[44]		
Units: Percentage change				
arithmetic mean (standard deviation)				
Serum or Plasma Cholesterol, Week 24, n=298, 310	5.0 (± 16.85)	-4.5 (± 15.44)		
Serum or Plasma Cholesterol, Week 48, n=298, 307	9.3 (± 17.10)	-3.3 (± 14.61)		
HDL Cholesterol, Direct, Week 24, n=299, 310	13.9 (± 25.17)	7.2 (± 32.22)		
HDL Cholesterol, Direct, Week 48, n=299, 307	15.3 (± 23.75)	4.0 (± 21.86)		
LDL Cholesterol, Week 24, n=298, 309	3.8 (± 25.85)	-7.8 (± 21.13)		
LDL Cholesterol, Week 48, n=297, 307	10.7 (± 27.54)	-4.1 (± 20.39)		
Triglycerides ,Week 24, n=299, 310	7.0 (± 40.45)	0.5 (± 44.01)		
Triglycerides , Week 48, n=299, 307	7.3 (± 46.92)	-0.3 (± 49.22)		

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 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) Lipid last observation carried forwardd (LOCF) data was used such that the last available fasted, on-treatment lipid value prior to the initiation of a lipid-lowering agent is used in place of future observed values. Participants on lipid-lowering agents at Baseline are excluded. 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	360[45]	359[46]		
Units: Percentage change				
arithmetic mean (standard deviation)				
Total/HDL Cholesterol Ratio, Week 24, n=298, 310	-4.4 (± 22.53)	-7.5 (± 17.90)		
Total/HDL Cholesterol Ratio, Week 48, n=298, 307	-2.8 (± 17.86)	-4.5 (± 18.25)		

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). 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 were 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 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	360[47]	359[48]		
Units: Percentage of participants				
Week 24, n=313, 320	4	0		
Week 48, n=324, 332	4	2		

Notes:

[47] - Safety Population

[48] - Safety Population

Statistical analyses

Statistical analysis title	Stat 1
Statistical analysis description:	
Week 24	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	3.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.5
upper limit	5.6

Statistical analysis title	Stat 2
Statistical analysis description:	
Week 48	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.037 [49]
Method	Fisher exact
Parameter estimate	Mean difference (final values)
Point estimate	2.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	5.4

Notes:

[49] - 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 invetigational 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 cells/mm3, >200 cells/mm3 for group-1), Baseline HIV-1 RNA (<=100000, >100000 c/mL) and

Race (White, African American/African heritage, 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	360[50]	359[51]		
Units: Percentage of participants				
Baseline CD4+ cell count Group-1, <=200,n=32,26	78	92		
Baseline CD4+ cell count Group-1, >200,n=328,333	95	94		
Female, n=54, 46	93	89		
Male, n=306, 313	94	95		
Age, <35,n= 209, 203	93	94		
Age, 35 to <50,n=115, 122	96	94		
Age, >=50, n=36, 34	94	91		
Baseline plasma HIV-1 RNA, <=100000,n=294,282	94	95		
Baseline plasma HIV-1 RNA, >100000,n=66, 77	92	90		
Race, White, n=237,249	95	95		
Race, African American/African H., n=55, 40	89	90		
Race, Asian, n=34, 30	97	90		
Race, Other, n=34, 40	91	93		

Notes:

[50] - ITT-E Population

[51] - 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 invetigational 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 cells/mm3, >200 cells/mm3 for group-1), Baseline HIV-1 RNA (<=100000, >100000) and Race (White, African American/African H., Asian and 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	360[52]	359[53]		
Units: Percentage of participants				
Baseline CD4+ cell count Group-1, <=200,n=32, 26	78	96		
Baseline CD4+ cell count Group-1, >200,n=328,333	95	94		
Female, n=54, 46	89	87		
Male, n=306, 313	94	95		
Age, <35,n= 209,203	92	94		
Age, 35 to <50,n=115, 122	97	94		
Age, >=50, n=36, 34	89	94		
Baseline plasma HIV-1 RNA, <=100000,n=294,282	92	95		
Baseline plasma HIV-1 RNA, >100000,n=66, 77	97	90		
Race, White, n=237,249	96	96		
Race, African American/African H., n=55, 40	80	88		
Race, Asian, n=34, 30	97	90		
Race, Other, n=34, 40	88	90		

Notes:

[52] - ITT-E Population

[53] - 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 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 the the latest pre-dose assessment. Change from Baseline was defined as value at the inidicated time point 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.

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	360	359		
Units: Cells/mm^3				
least squares mean (standard error)				
Baseline plasma HIV-1 RNA,<=100000, n=273,271	215.6 (± 10.67)	208.7 (± 10.71)		
Baseline plasma HIV-1 RNA,>100000, n=64,69	261.8 (± 22.27)	248.7 (± 21.30)		
Baseline CD4+ cell count,<=200, n=28, 25	210.9 (± 33.42)	153.2 (± 35.29)		
Baseline CD4+ cell count,>200, n=309, 315	225.8 (± 10.00)	221.7 (± 9.89)		
Age group-1, <35,n= 193, 191	234.2 (± 12.67)	201.7 (± 12.72)		
Age group-1, 35 to <50, n=112, 117	212.7 (± 16.59)	244.2 (± 16.31)		
Age group-1, >=50, n=32, 32	209.1 (± 31.20)	203.9 (± 31.06)		
Age group-2, <50,n= 305, 308	226.4 (± 10.09)	217.8 (± 10.03)		
Age group-2, >=50, n= 32, 32	208.5 (± 31.27)	204.1 (± 31.14)		
Female, n=48, 41	236.2 (± 25.35)	263.6 (± 27.50)		
Male, n=289, 299	222.8 (± 10.33)	210.0 (± 10.17)		
Race group, White, n=227, 241	223.3 (± 11.70)	214.2 (± 11.38)		
Race group, African Am/African H., n=45, 36	214.0 (± 26.25)	233.7 (± 29.39)		
Race group, Asian, n=33, 27	205.0 (± 30.92)	189.3 (± 33.90)		
Race group, Other, n=32, 36	270.2 (± 31.16)	235.3 (± 29.47)		

Statistical analyses

Statistical analysis title	Stat 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, Baseline plasma HIV-1 RNA, and treatment and relevant Baseline plasma HIV-1 RNA interaction.

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

Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	6.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.7
upper limit	36.6

Statistical analysis title	Stat 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, Baseline plasma HIV-1 RNA, and treatment and Baseline plasma HIV-1 RNA interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	13.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-46.8
upper limit	73.2

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	57.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-37.2
upper limit	152.5

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	4.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.5
upper limit	31.7

Statistical analysis title	Stat 5
Statistical analysis description:	
Age Group-1,<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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	32.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	67.7

Statistical analysis title	Stat 6
Statistical analysis description:	
Age Group-1,35 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-31.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-77.1
upper limit	14.2

Statistical analysis title	Stat 7

Statistical analysis description:

Age Group-1,>=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	719
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	-81.4
upper limit	91.8

Statistical analysis title	Stat 10

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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-27.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-100.8
upper limit	46.1

Statistical analysis title	Stat 11

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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	12.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.7
upper limit	41.2

Statistical analysis title	Stat 12
Statistical analysis description:	
Race group-white. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	9.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.9
upper limit	41.1

Statistical analysis title	Stat 13
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, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
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	-97.1
upper limit	57.6

Statistical analysis title	Stat 14

Statistical analysis description:

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

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	15.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.4
upper limit	105.9

Statistical analysis title	Stat 15

Statistical analysis description:

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

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49
upper limit	119

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 and as HIV infection progresses, the number of these cells declines. It was evaluated by flow cytometry. Baseline value is the latest pre-dose assessment (Day 1). Change from Baseline was defined as value at the indicated time point 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 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	360[54]	359[55]		
Units: Cells/mm^3				
arithmetic mean (standard error)				
Baseline plasma HIV-1 RNA,<=100000, n=283,273	186.01 (± 9.948)	148.21 (± 10.134)		
Baseline plasma HIV-1 RNA,>100000, n=66,72	193.90 (± 20.811)	220.71 (± 19.814)		
Baseline CD4+ cell count,<=200, n=29, 26	167.95 (± 31.308)	106.23 (± 32.990)		
Baseline CD4+ cell count,>200, n=320, 319	189.91 (± 9.362)	167.35 (± 9.362)		
Age group, <35,n= 201, 193	190.12 (± 11.829)	151.13 (± 12.050)		
Age group-1, 35 to <50, n=113, 119	180.50 (± 15.733)	190.40 (± 15.404)		
Age group-1, >=50, n=32, 32	198.74 (± 28.411)	133.21 (± 29.120)		
Female, n=52, 42	213.58 (± 23.225)	153.92 (± 25.910)		
Male, n=297, 303	183.41 (± 9.719)	164.18 (± 9.631)		
Race group, White, n=233, 240	182.20 (± 10.987)	168.30 (± 10.846)		
Race group, African Am/African H., n=51, 39	214.17 (± 23.472)	145.44 (± 26.841)		
Race group, Asian, n=33, 28	154.14 (± 29.401)	141.22 (± 31.663)		
Race group, Other, n=32, 38	222.24 (± 29.643)	163.05 (± 27.293)		

Notes:

[54] - ITT-E Population.

[55] - ITT-E Population.

Statistical analyses

Statistical analysis title	Stat 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, Baseline plasma HIV-1 RNA, and treatment and relevant Baseline plasma HIV-1 RNA interaction.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	37.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.98
upper limit	65.62

Statistical analysis title	Stat 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, Baseline plasma HIV-1 RNA, and treatment and Baseline plasma HIV-1 RNA interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-26.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-82.72
upper limit	29.1

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	61.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.94
upper limit	150.39

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Median difference (net)
Point estimate	22.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.42
upper limit	48.55

Statistical analysis title	Stat 5

Statistical analysis description:

Age Group,<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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	38.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.88
upper limit	72.09

Statistical analysis title	Stat 6

Statistical analysis description:

Age Group,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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	-9.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.1
upper limit	33.3

Statistical analysis title	Stat 7

Statistical analysis description:

Age Group,>=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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	65.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.43
upper limit	145.5

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	59.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.62
upper limit	127.94

Statistical analysis title	Stat 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	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	19.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.65
upper limit	46.1

Statistical analysis title	Stat 10
Statistical analysis description:	
Race group-white. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	13.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.35
upper limit	44.15

Statistical analysis title	Stat 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, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	68.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.24
upper limit	138.72

Statistical analysis title	Stat 12
Statistical analysis description:	
Race group-Asian. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	12.93

Confidence interval	
level	95 %
sides	2-sided
lower limit	-71.9
upper limit	97.75

Statistical analysis title	Stat 13
Statistical analysis description:	
Race group-Other. Following covariates/factors were adjusted: Treatment, Baseline plasma HIV-1 RNA (factor), Baseline CD4+ cell count, race, and treatment and race interaction.	
Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Mean difference (net)
Point estimate	59.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.73
upper limit	138.11

Secondary: Change from Baseline in European Quality of Life (EuroQoL) – 5 Dimensions – 5 Levels (EQ-5D-5L) utility score at Weeks 4, 24 48

End point title	Change from Baseline in European Quality of Life (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 5-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, 2=slight , 3=moderate, 4=severe 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. MMRM was run on LOCF dataset. 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 (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	360[56]	359[57]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 4, n=359, 355	0.0111 (± 0.00326)	0.0130 (± 0.00510)		
Week 24, n=360, 358	0.0207 (± 0.00310)	0.0203 (± 0.00347)		
Week 48, n=360, 358	0.0189 (± 0.00362)	0.0208 (± 0.00342)		

Notes:

[56] - ITT-E Population.

[57] - ITT-E Population.

Statistical analyses

Statistical analysis title	Stat 1

Statistical analysis description:

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

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.759
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.0019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0137
upper limit	0.01

Statistical analysis title	Stat 2

Statistical analysis description:

Week 24. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA , Baseline CD4+ cell count, and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit as factors and covariate, with visit as the repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.943
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	0.0003

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0088
upper limit	0.0095

Statistical analysis title	Stat 3

Statistical analysis description:

Week 48. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA , Baseline CD4+ cell count, and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit as factors and covariate, with visit as the repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.703
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.0019
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0117
upper limit	0.0079

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 5-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	360[58]	359[59]		
Units: Scores on a scale				
least squares mean (standard error)				
Week 4, n=358, 355	1.8 (± 0.50)	3.1 (± 0.41)		
Week 24, n=359, 358	3.9 (± 0.43)	4.5 (± 0.48)		
Week 48, n=359, 358	4.0 (± 0.43)	4.6 (± 0.48)		

Notes:

[58] - ITT-E Population.

[59] - ITT-E Population.

Statistical analyses

Statistical analysis title	Stat 1

Statistical analysis description:

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

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.045
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.6
upper limit	0

Statistical analysis title	Stat 2

Statistical analysis description:

Week 24. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA, Baseline CD4+ cell count and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit as factors and covariate, with visit as the repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.358
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.7

Statistical analysis title	Stat 3

Statistical analysis description:

Week 48. Covariates adjusted: Treatment, Baseline plasma HIV-1 RNA, Baseline CD4+ cell count, and Baseline EQ-5D utility, treatment*visit and Baseline EQ-5D utility*visit as factors and covariate, with visit as the
repeated factor.

Comparison groups	DTG + 3TC v DTG + TDF/FTC
Number of subjects included in analysis	719
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.328
Method	MMRM
Parameter estimate	Mean difference (net)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.6

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Post-Baseline SAEs and non-SAEs 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 + 3TC
Reporting group description:	
Participants received a two-drug regimen of DTG + 3TC administered orally, once daily for 48 weeks.	
Reporting group title	DTG + TDF/FTC
Reporting group description:	
Participants received a three-drug regimen of DTG + TDF/FTC FDC administered orally, once daily for 48 weeks.	

Serious adverse events	DTG + 3TC	DTG + TDF/FTC	
Total subjects affected by serious adverse events			
subjects affected / exposed	29 / 360 (8.06%)	33 / 359 (9.19%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 360 (0.56%)	3 / 359 (0.84%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal cancer stage 0			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Basal cell carcinoma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burkitt's lymphoma			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (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			
Contusion			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture of penis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lower limb fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penetrating abdominal trauma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (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			
Sciatica			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Ophthalmic vein thrombosis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (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	0 / 360 (0.00%)	2 / 359 (0.56%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	3 / 360 (0.83%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 360 (0.28%)	2 / 359 (0.56%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Acute psychosis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic psychosis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urethral meatus stenosis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (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			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Hepatitis A			
subjects affected / exposed	3 / 360 (0.83%)	3 / 359 (0.84%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis C			
subjects affected / exposed	1 / 360 (0.28%)	1 / 359 (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 / 360 (0.28%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal abscess			

subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Salmonellosis			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue infection			
subjects affected / exposed	0 / 360 (0.00%)	1 / 359 (0.28%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	1 / 360 (0.28%)	0 / 359 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DTG + 3TC	DTG + TDF/FTC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	189 / 360 (52.50%)	215 / 359 (59.89%)	
Nervous system disorders			
Headache			
subjects affected / exposed	31 / 360 (8.61%)	31 / 359 (8.64%)	
occurrences (all)	38	36	
Dizziness			
subjects affected / exposed	7 / 360 (1.94%)	13 / 359 (3.62%)	
occurrences (all)	9	14	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	10 / 360 (2.78%)	6 / 359 (1.67%)	
occurrences (all)	12	6	
Influenza like illness			
subjects affected / exposed	10 / 360 (2.78%)	6 / 359 (1.67%)	
occurrences (all)	11	6	
Pyrexia			
subjects affected / exposed	8 / 360 (2.22%)	5 / 359 (1.39%)	
occurrences (all)	8	6	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	35 / 360 (9.72%)	35 / 359 (9.75%)	
occurrences (all)	40	38	
Nausea			

subjects affected / exposed	15 / 360 (4.17%)	23 / 359 (6.41%)	
occurrences (all)	15	24	
Abdominal pain			
subjects affected / exposed	6 / 360 (1.67%)	12 / 359 (3.34%)	
occurrences (all)	6	13	
Haemorrhoids			
subjects affected / exposed	8 / 360 (2.22%)	10 / 359 (2.79%)	
occurrences (all)	8	10	
Constipation			
subjects affected / exposed	8 / 360 (2.22%)	8 / 359 (2.23%)	
occurrences (all)	9	8	
Toothache			
subjects affected / exposed	7 / 360 (1.94%)	9 / 359 (2.51%)	
occurrences (all)	7	9	
Vomiting			
subjects affected / exposed	8 / 360 (2.22%)	8 / 359 (2.23%)	
occurrences (all)	8	8	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	11 / 360 (3.06%)	9 / 359 (2.51%)	
occurrences (all)	13	9	
Cough			
subjects affected / exposed	7 / 360 (1.94%)	8 / 359 (2.23%)	
occurrences (all)	7	8	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 360 (1.11%)	10 / 359 (2.79%)	
occurrences (all)	4	11	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	11 / 360 (3.06%)	16 / 359 (4.46%)	
occurrences (all)	11	19	
Anxiety			
subjects affected / exposed	9 / 360 (2.50%)	11 / 359 (3.06%)	
occurrences (all)	9	11	
Depression			

subjects affected / exposed	6 / 360 (1.67%)	8 / 359 (2.23%)	
occurrences (all)	6	8	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	8 / 360 (2.22%)	2 / 359 (0.56%)	
occurrences (all)	8	2	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	16 / 360 (4.44%)	12 / 359 (3.34%)	
occurrences (all)	18	14	
Arthralgia			
subjects affected / exposed	10 / 360 (2.78%)	15 / 359 (4.18%)	
occurrences (all)	11	15	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 360 (6.11%)	41 / 359 (11.42%)	
occurrences (all)	28	47	
Upper respiratory tract infection			
subjects affected / exposed	32 / 360 (8.89%)	22 / 359 (6.13%)	
occurrences (all)	38	26	
Pharyngitis			
subjects affected / exposed	13 / 360 (3.61%)	19 / 359 (5.29%)	
occurrences (all)	15	19	
Influenza			
subjects affected / exposed	8 / 360 (2.22%)	17 / 359 (4.74%)	
occurrences (all)	8	19	
Syphilis			
subjects affected / exposed	10 / 360 (2.78%)	12 / 359 (3.34%)	
occurrences (all)	12	12	
Respiratory tract infection viral			
subjects affected / exposed	11 / 360 (3.06%)	9 / 359 (2.51%)	
occurrences (all)	13	13	
Bronchitis			
subjects affected / exposed	8 / 360 (2.22%)	10 / 359 (2.79%)	
occurrences (all)	9	11	
Gastroenteritis			

subjects affected / exposed	7 / 360 (1.94%)	11 / 359 (3.06%)	
occurrences (all)	7	13	
Tonsillitis			
subjects affected / exposed	10 / 360 (2.78%)	8 / 359 (2.23%)	
occurrences (all)	10	9	
Gonorrhoea			
subjects affected / exposed	9 / 360 (2.50%)	7 / 359 (1.95%)	
occurrences (all)	9	8	
Chlamydial infection			
subjects affected / exposed	7 / 360 (1.94%)	8 / 359 (2.23%)	
occurrences (all)	8	8	
Rhinitis			
subjects affected / exposed	2 / 360 (0.56%)	9 / 359 (2.51%)	
occurrences (all)	2	9	
Genital herpes			
subjects affected / exposed	1 / 360 (0.28%)	8 / 359 (2.23%)	
occurrences (all)	1	12	
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	8 / 360 (2.22%)	4 / 359 (1.11%)	
occurrences (all)	8	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 November 2017	The double barrier method of contraception (male condom combined with a vaginal spermicide) was added 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 DTG use. Assessment of inflammation biomarkers ([interleukin {IL}-6, high sensitivity C-reactive protein {hs-CRP}) at Day 1, and Weeks 48, 96 and 144, and Assessment of telomere length at Day 1, and Weeks 96 and 144, were added as new exploratory endpoints. For clarification purposes, the peripheral blood mononuclear cell (PBMC) sample in Section 7.1 (Time and Events table) and Section 7.6.1 (Human immuno deficiency virus [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 DTG tablets was added to Section 6.1 (Investigational Product and Other Study Treatment) to allow use of commercial material as well as clinical trial material. The physical description for open-label lamivudine in Section 6.1 was corrected. Standard procedures for forwarding pregnancy information to the Antiretroviral Pregnancy Register were added. For clarification purposes, the AE severity grading's in Appendix 7, Section 12.7.6 (Evaluating AEs and SAEs) were updated to be consistent with Appendix 6, Section 12.6. (Division of AIDS table for Grading Severity of Adult and Pediatric AEs). This change has no impact on the investigators evaluation of AEs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported