Clinical trial results:
A Phase III, randomized, multicenter, parallel-group, non-inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus lamivudine in HIV-1 infected adults who are virologically suppressed

Summary

EudraCT number	2015-004401-17
Trial protocol	DE GB ES BE NL
Global end of trial date	

Results information

Result version number	v3
This version publication date	18 April 2022
First version publication date	02 May 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	204862

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	06 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 May 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferior antiviral activity of switching to DTG +3TC once daily compared to continuation of TBR over 48 weeks in HIV-1 infected, ART therapy (ART)-experienced, virologically suppressed participants.

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 40
Country: Number of subjects enrolled	Belgium: 25
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 83
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 229
Country: Number of subjects enrolled	United States: 286
Country: Number of subjects enrolled	United Kingdom: 13
Worldwide total number of subjects	743
EEA total number of subjects	368

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)	726
From 65 to 84 years	17
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This non-inferiority study evaluated antiviral activity of switching to dolutegravir (DTG) + lamivudine (3TC) fixed dose combination (FDC) once daily compared to continuation of a Tenofovir alafenamide (TAF)-based regimen (TBR) over 48 weeks in virologically suppressed participants with human immunodeficiency type 1 infection.

Pre-assignment

Screening details:

743 participants were enrolled, of which two participants did not receive treatment and hence 741 participants received at least one treatment into the study. The results presented are based on Week 48 primary analysis.

Period 1

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

Arms

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

Arm description:

Participants who were on a stable TBR and who had an HIV-1 ribonucleic acid (RNA) <50 copies per millilter (c/mL) at the time of screening, received fixed dose combination of DTG 50 milligrams (mg) + 3TC 300 mg once daily up to 48 weeks.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir (DTG)+Lamivudine (3TC) fixed dose combination (FDC)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received DTG 50 milligrams (mg) + 3TC 300 mg FDC as a white, oval and film-coated tablet. The tablets were packed in high density polyethylene (HDPE) bottles with induction seals, 2 grams (gm) desiccant, and child resistant closures. Each 60 milliliter (mL) bottle contains 30 tablets.

Arm title	TAF-based regimen

Arm description:

Participants who were on a stable TBR and who had an HIV-1 RNA<50 c/mL at the time of screening, were continued to receive TBR up to 48 weeks. One participant randomized to the TBR arm received TDF (tenofovir disoproxil) rather than TAF-and was presented within the "TAF-based regimen" arm for efficacy because the efficacy of TAF and TDF are comparable. However the participant was presented separately under "TDF-based regimen" for Safety because the safety profiles of TDF and TAF differ.

Arm type	Active comparator
Investigational medicinal product name	Tenofovir alafenamide (TAF) based regimen (TBR)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants continued to receive stable TBR

Number of subjects in period 1[1]	DTG+3TC FDC	TAF-based regimen
Started	369	372
Completed	0	0
Not completed	369	372
Physician decision	1	1
Consent withdrawn by subject	7	16
Adverse event, non-fatal	13	2
Ongoing at the time of interim analysis	342	343
Lost to follow-up	3	5
Protocol deviation	3	2
Lack of efficacy	-	3

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: Two participants out of the total number of participants enrolled did not receive treatment.

Baseline characteristics

Reporting groups	
Reporting group title	DTG+3TC FDC
Reporting group description:	
Participants who were on a stable TBR and who had an HIV-1 ribonucleic acid (RNA) <50 copies per millilter (c/mL) at the time of screening, received fixed dose combination of DTG 50 milligrams (mg) + 3TC 300 mg once daily up to 48 weeks.	
Reporting group title	TAF-based regimen
Reporting group description:	
Participants who were on a stable TBR and who had an HIV-1 RNA<50 c/mL at the time of screening, were continued to receive TBR up to 48 weeks. One participant randomized to the TBR arm received TDF (tenofovir disoproxil) rather than TAF-and was presented within the "TAF-based regimen" arm for efficacy because the efficacy of TAF and TDF are comparable. However the participant was presented separately under "TDF-based regimen" for Safety because the safety profiles of TDF and TAF differ.	

Reporting group values	DTG+3TC FDC	TAF-based regimen	Total
Number of subjects	369	372	741
Age categorical Units: Subjects			
All Participants	369	372	741
Age Continuous Units: Years			
arithmetic mean	40.6	40.9	
standard deviation	± 10.76	± 11.54	-
Sex: Female, Male Units: Participants			
Female	25	33	58
Male	344	339	683
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	7	8	15
Asian-Central/South Asian Heritage (H)	3	4	7
Asian-Japanese H/East Asian H/South East Asian H	10	9	19
Black or African American	50	58	108
Native Hawaiian or other Pacific Islander	1	3	4
White-Arabic/North African (NA) H	5	2	7
White-Arabic/NA H and white/caucasia/European H	0	1	1
White-White/caucasian/European H	292	286	578
Asian and White	0	1	1
Black or African American and White	1	0	1
Baseline third agent			
Blood samples were collected to evaluate Baseline third agents including non-nucleoside reverse transcriptase inhibitors (NNRTI), integrase strand transfer inhibitors (INSTI) and protease inhibitors (PI) based on the antiretroviral medications taken at Baseline.			
Units: Subjects			
NNRTI	51	48	99
INSTI	289	296	585

Protease Inhibiitors	29	28	57
HIV infection by Centers for Disease Control and Prevention (CDC) classification			
CDC classification for human immunodeficiency (HIV) were: Stage 1: No acquired immuno deficiency syndrome (AIDS) defining condition and CD4+ T-lymphocyte count: >=500 cells per microliter (cells/mcL); Stage 2: No AIDS infection and CD4+ lymphocyte count: 200-499 cell/mcL and Stage 3: with HIV infection and CD4+ T-lymphocye count <200 cells/mcL.			
Units: Subjects			
HIV infection Stage 1	255	259	514
HIV infection Stage 2	94	94	188
HIV infection Stage 3	20	19	39
Cluster of differentiation 4 plus (CD4+) cell count			
Blood samples were collected to evaluate Baseline CD4+ cell count using flow cytometry. Median along with first and third quartiles are presented for Baseline CD4+ count.			
Units: Cells per cubic millimeter (cells/mm^3)			
median	682.0	720.0	
inter-quartile range (Q1-Q3)	492.0 to 862.0	531.5 to 901.5	-

Subject analysis sets

Subject analysis set title	Randomized to TBR but received TDF-based regimen
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participant randomized to TBR arm who had HIV-1 RNA <50 c/mL at the time of screening, received TDF-based regimen instead of TAF-based regimen in error. Participant continued to receive TDF-regimen up to the Week 48 visit (participant withdrew from the study at Week 36)

Reporting group values	Randomized to TBR but received TDF-based regimen		
Number of subjects	1		
Age categorical			
Units: Subjects			
All Participants	1		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	±		
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native			
Asian-Central/South Asian Heritage (H)			
Asian-Japanese H/East Asian H/South East Asian H			
Black or African American			
Native Hawaiian or other Pacific Islander			
White-Arabic/North African (NA) H			

White-Arabic/NA H and white/caucasia/European H White-White/caucasian/European H Asian and White Black or African American and White			
Baseline third agent			
Blood samples were collected to evaluate Baseline third agents including non-nucleoside reverse transcriptase inhibitors (NNRTI), integrase strand transfer inhibitors (INSTI) and protease inhibitors (PI) based on the antiretroviral medications taken at Baseline.			
Units: Subjects			
NNRTI INSTI Protease Inhibiitors			
HIV infection by Centers for Disease Control and Prevention (CDC) classification			
CDC classification for human immunodeficiency (HIV) were: Stage 1: No acquired immuno deficiency syndrome (AIDS) defining condition and CD4+ T-lymphocyte count: >=500 cells per microliter (cells/mcL); Stage 2: No AIDS infection and CD4+ lymphocyte count: 200-499 cell/mcL and Stage 3: with HIV infection and CD4+ T-lymphocye count <200 cells/mcL.			
Units: Subjects			
HIV infection Stage 1 HIV infection Stage 2 HIV infection Stage 3			
Cluster of differentiation 4 plus (CD4+) cell count			
Blood samples were collected to evaluate Baseline CD4+ cell count using flow cytometry. Median along with first and third quartiles are presented for Baseline CD4+ count.			
Units: Cells per cubic millimeter (cells/mm^3) median inter-quartile range (Q1-Q3)			

End points

End points reporting groups

Reporting group title	DTG+3TC FDC

Reporting group description:

Participants who were on a stable TBR and who had an HIV-1 ribonucleic acid (RNA) <50 copies per millilter (c/mL) at the time of screening, received fixed dose combination of DTG 50 milligrams (mg) + 3TC 300 mg once daily up to 48 weeks.

Reporting group title	TAF-based regimen

Reporting group description:

Participants who were on a stable TBR and who had an HIV-1 RNA<50 c/mL at the time of screening, were continued to receive TBR up to 48 weeks. One participant randomized to the TBR arm received TDF (tenofovir disoproxil) rather than TAF-and was presented within the "TAF-based regimen" arm for efficacy because the efficacy of TAF and TDF are comparable. However the participant was presented separately under "TDF-based regimen" for Safety because the safety profiles of TDF and TAF differ.

Subject analysis set title	Randomized to TBR but received TDF-based regimen
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participant randomized to TBR arm who had HIV-1 RNA <50 c/mL at the time of screening, received TDF-based regimen instead of TAF-based regimen in error. Participant continued to receive TDF-regimen up to the Week 48 visit (participant withdrew from the study at Week 36)

Primary: Percentage of participants with virologic failure endpoint as per Food and Drug Administration (FDA) snapshot category at Week 48

End point title	Percentage of participants with virologic failure endpoint as per Food and Drug Administration (FDA) snapshot category at Week 48

End point description:

Percentage of participants with virologic failure (plasma HIV-1 RNA >=50 c/mL) was evaluated using FDA snapshot algorithm at Week 48. The Snapshot algorithm treated all participants without HIV-1 RNA data at the visit of interest (due to missing data or discontinuation of investigational product prior to the visit window) as non-responders, as well as participants who switch their concomitant antiretroviral therapy (ART) prior to the visit of interest. Intent-to-treat exposed (ITT-E) Population comprises of all randomized participants who receive at least one dose of study treatment either DTG + 3TC or TBR. Participants were assessed according to the treatment to which the participant was randomized. Any participant receiving a treatment randomization number was considered to be randomized. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Primary

End point timeframe:

Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[1]	372[2]		
Units: Percentage of participants				
number (not applicable)	0.3	0.5		

Notes:

[1] - ITT-E Population.

[2] - ITT-E Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ADP was based on Cochran-Mantel Haenszel stratified analysis adjusting for Baseline stratification factor: Baseline third agent (PI, NNRTI, and INSTI).

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	741
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Adjusted difference in proportion (ADP)
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	0.7

Notes:

[3] - Non-inferiority of switching to DTG + 3TC compared to continuation of TBR (as per FDA snapshot algorithm) was to be concluded if the upper bound of a two-sided 95% confidence interval (CI) for the difference in virologic failure rates between the two treatment arms was smaller than 4%.

Secondary: Percentage of participants with plasma HIV-1 RNA <50 c/mL as per snapshot algorithm at Week 48

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL as per snapshot algorithm at Week 48

End point description:

Percentage of participants with plasma HIV-1 RNA <50 c/mL (virologic success) was evaluated using FDA snapshot algorithm at Week 48 to demonstrate the non-inferior antiviral activity of switching to DTG +3TC once daily compared to continuation of TBR over 48 weeks. 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. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[4]	372[5]		
Units: Percentage of participants				
number (not applicable)	93.2	93.0		

Notes:

[4] - ITT-E Population.

[5] - ITT-E Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

ADP was based on Cochran-Mantel Haenszel stratified analysis adjusting for Baseline stratification factor: Baseline third agent (PI, NNRTI, and INSTI).

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	741
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Adjusted difference in proportion
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	3.9

Notes:

[6] - Non-inferiority of switching to DTG + 3TC compared to continuation of TBR (as per FDA snapshot algorithm) was to be concluded when the lower bound of a 2-sided 95% confidence interval for the difference in success rates between the two treatment arms was greater than -8%.

Secondary: Percentage of participants with virologic failure endpoint as per FDA snapshot category at Week 24

End point title	Percentage of participants with virologic failure endpoint as per FDA snapshot category at Week 24

End point description:

Percentage of participants with plasma HIV-1 RNA >=50 c/mL was evaluated using FDA snapshot algorithm at Week 24. 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. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

Week 24

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[7]	372[8]		
Units: Percentage of participants				
number (not applicable)	0.3	0.8		

Notes:

[7] - ITT-E Population.

[8] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Percentage of participants with plasma HIV-1 RNA <50 c/mL was evaluated using FDA snapshot algorithm at Week 24. 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. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

Week 24

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[9]	372[10]		
Units: Percentage of participants	95	96		

Notes:

[9] - ITT-E Population.

[10] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ cell count at Weeks 24 and 48

End point title	Change from Baseline in CD4+ cell count at Weeks 24 and 48

End point description:

CD4+ cells are type of white blood cells that fight infection and as HIV infection progresses, the number of these cells declines. Blood samples were collected at specified time points to assess CD4+. It was evaluated by flow cytometry. Baseline value is defined as the latest pre-dose assessment with a non-missing value (Day 1). Change from Baseline is defined as post-dose visit value minus Baseline value. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable. All 741 (369+372) participants were analyzed, however only those participants with data available at the specified data 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 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[11]	372[12]		
Units: Cells per cubic millimeter				
median (inter-quartile range (Q1-Q3))				
Week 24, n=351, 359	21.0 (-68.0 to 115.0)	6.0 (-87.0 to 99.0)		
Week 48, n=344, 345	22.5 (-71.0 to 121.5)	11.0 (-98.0 to 90.0)		

Notes:

[11] - ITT-E Population.

[12] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+/CD8+ cell count ratio at Weeks 24 and 48

End point title	Change from Baseline in CD4+/CD8+ cell count ratio at Weeks 24 and 48

End point description:

Blood samples were collected at specified time points to assess CD4+/CD8+ cell count ratio. It was assessed by flow cyclometry to evaluate the immunologic activity of switching to DTG+3TC once daily compared to continuation of TBR over 48 Weeks. Baseline (Day 1) values were the actual CD4+ cell count ratio values at pre-dose Day 1. Change from Baseline is defined as post-dose visit value minus Baseline value. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable. All 741 (369+372) participants were analyzed, however only those participants with data available at the specified data 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 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[13]	372[14]		
Units: Ratio				
median (inter-quartile range (Q1-Q3))				
Baseline (Day 1), n=366, 371	0.950 (0.710 to 1.250)	0.960 (0.730 to 1.310)		
Week 24, n=346, 358	0.010 (-0.070 to 0.110)	0.040 (-0.060 to 0.120)		
Week 48, n=342, 343	0.030 (-0.050 to 0.110)	0.050 (-0.050 to 0.160)		

Notes:

[13] - ITT-E Population.

[14] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with disease progression at Weeks 24 and 48

End point title	Number of participants with disease progression at Weeks 24 and 48

End point description:

HIV-associated conditions were recorded during the study and was assessed according to the 2014 CDC Classification System for HIV Infection in Adults. CDC classification for HIV were: Stage 1: No AIDS defining condition and CD4+ T-lymphocyte count: >=500 cells/mcL; Stage 2: No AIDS infection and CD4+ lymphocyte count: 200-499 cell/mcL and Stage 3: with HIV infection and CD4+ T-lymphocye count <200 cells/mcL. Disease progression summarize participants who had HIV infection stage 3 associated conditions or death. Indicators of clinical disease progression were defined as: CDC Category Stage 1 at enrolment to Stage 3 event; CDC Category Stage 2 at enrolment to Stage 3 event; CDC Category Stage 3 at enrolment to New Stage 3 Event; CDC Category Stage 1, 2 or 3 at enrolment to Death. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

At Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[15]	372[16]		
Units: Participants				
From CDC Stage 1 to CDC Stage 3 Event	1	0		
From CDC Stage 2 to CDC Stage 3 Event	0	0		
From CDC Stage 3 to new CDC Stage 3 Event	0	0		
From CDC Stage 1, 2 or 3 to Death	1	0		
No HIV-1 disease progression	367	372		

Notes:

[15] - ITT-E Population.

[16] - ITT-E Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any serious adverse events (SAEs) and common (>=2%) non-serious adverse events (non-SAEs)

End point title	Number of participants with any serious adverse events (SAEs) and common (>=2%) non-serious adverse events (non-SAEs)

End point description:

An AE is any untoward medical occurrence temporally associated with use of a study treatment, whether or not considered related to study treatment. A SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, associated with liver injury and impaired liver function or any other situations as per medical or scientific judgment. Safety Population included participants who received at least 1 dose of study treatment and was based on treatment the participant actually received. One participant randomized to TBR but received TDF-based regimen and because safety profiles of TDF and TAF differ, this participant was removed from overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[17]	371[18]		
Units: Participants				
Any non-SAE (>=2%)	222	204		
Any SAE	21	16		

Notes:

[17] - Safety Population.

[18] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants randomized to TBR arm receiving TDF-based regimen with any SAEs and common (>=2%) non-SAEs

End point title	Number of participants randomized to TBR arm receiving TDF-based regimen with any SAEs and common (>=2%) non-SAEs

End point description:

An AE is any untoward medical occurrence temporally associated with the use of a study treatment, whether or not considered related to study treatment. A SAE is any untoward medical occurrence that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability/incapacity, is a congenital anomaly/birth defect, associated with liver injury and impaired liver function or any other situations as per medical or scientific judgment. Number of TDF-based regimen participants with any SAE and common (>=2%) non-SAEs are presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[19]			
Units: Participants				
Any non-SAE (>=2%)	1			
Any SAE	0			

Notes:

[19] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with AEs by their severity Grades

End point title	Number of Participants with AEs by their severity Grades

End point description:

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

participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[20]	371[21]		
Units: Participants				
Grade 1	102	94		
Grade 2	170	177		
Grade 3	19	15		
Grade 4	3	6		
Grade 5	1	0		

Notes:

[20] - Safety Population.

[21] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants randomized to TBR arm receiving TDF-based regimen with AEs by their severity Grades

End point title	Number of participants randomized to TBR arm receiving TDF-based regimen with AEs by their severity Grades

End point description:

An AE is any untoward medical occurrence in a clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Adverse events were evaluated by the investigator and graded according to the 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 TDF-based regimen participants with adverse events by maximum grade have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[22]			
Units: Participants				
Grade 1	0			

Grade 2	1			
Grade 3	0			
Grade 4	0			
Grade 5	0			

Notes:

[22] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued the treatment due to AEs

End point title	Number of participants who discontinued the treatment due to AEs

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Number of participants who discontinued the treatment due to adverse events have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[23]	371[24]		
Units: Participants	13	2		

Notes:

[23] - Safety Population.

[24] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants randomized to TBR arm receiving TDF-based regimen who discontinued the treatment due to AEs

End point title	Number of participants randomized to TBR arm receiving TDF-based regimen who discontinued the treatment due to AEs

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study treatment, whether or not considered related to the study treatment. Number of participants who discontinued the treatment due to adverse events have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[25]			
Units: Participants	0			

Notes:

[25] - 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 the analysis of hematology parameters-platelet count, neutrophils, hemoglobin and leukocytes. Any abmormality in hematology parameters were evaluated according to the DAIDS toxicity scale from Grade 1 to 4: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe) and Grade 4 (Potentially life-threatening). The higher the grade, the more severe the symptoms. Only those participants with maximum post-Baseline emergent hematology toxicities in any of the hematology parameters have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[26]	371[27]		
Units: Participants				
Hemoglobin, Grade 1	3	0		
Hemoglobin, Grade 2	0	0		
Hemoglobin, Grade 3	0	0		
Hemoglobin, Grade 4	0	0		
Leukocytes, Grade 1	1	1		
Leukocytes, Grade 2	1	0		
Leukocytes, Grade 3	0	0		
Leukocytes, Grade 4	0	0		
Neutrophils, Grade 1	3	4		
Neutrophils, Grade 2	2	4		
Neutrophils, Grade 3	0	0		

Neutrophils, Grade 4	1	0		
Platelets, Grade 1	6	5		
Platelets, Grade 2	1	1		
Platelets, Grade 3	0	0		
Platelets, Grade 4	0	0		

Notes:

[26] - Safety Population.

[27] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants randomized to TBR arm receiving TDF-based regimen with Maximum Post-Baseline emergent hematology toxicities

End point title	Number of participants randomized to TBR arm receiving TDF-based regimen with Maximum Post-Baseline emergent hematology toxicities

End point description:

Blood samples were collected up to the Week 36 visit for the analysis of hematology parameters-platelet count, neutrophils, hemoglobin and leukocytes. Any abnormality in hematology parameters were evaluated according to the DAIDS toxicity scale from Grade 1 to 4: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe) and Grade 4 (Potentially life-threatening). The higher the grade, the more severe the symptoms. Only those TDF-based regimen participants with maximum post-Baseline emergent hematology toxicities in any of the hematology parameters have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 36

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[28]			
Units: Participants				
Hemoglobin, Grade 1	0			
Hemoglobin, Grade 2	0			
Hemoglobin, Grade 3	0			
Hemoglobin, Grade 4	0			
Leukocytes, Grade 1	0			
Leukocytes, Grade 2	0			
Leukocytes, Grade 3	0			
Leukocytes, Grade 4	0			
Neutrophils, Grade 1	0			
Neutrophils, Grade 2	0			
Neutrophils, Grade 3	0			
Neutrophils, Grade 4	0			
Platelets, Grade 1	0			
Platelets, Grade 2	0			

Platelets, Grade 3	0			
Platelets, Grade 4	0			

Notes:

[28] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Maximum Post-Baseline emergent clinical chemistry toxicities

End point title	Number of participants with Maximum Post-Baseline emergent clinical chemistry toxicities

End point description:

Blood samples were collected for analysis of alanine aminotransferase(ALT), albumin, alkaline phosphate(ALP), aspartate aminotransferase(AST), bilirubin, carbon dioxide(CO2), cholesterol, creatinine kinase(CK), creatinine, direct bilirubin, glomerular filtration rate(GFR) from creatinine adjusted for body surface area(BSA), GFR from cystatin C adjusted using chronic kidney disease-epidemiology collaboration(CKD-EPI), hyper/hypocalcemia, hyper/hypo-glycemia, hyper/hypo-kalemia, hyper/hypo-natremia, low density lipoprotein(LDL) cholesterol, phosphate and triglycerides. Any abnormality was evaluated according to DAIDS toxicity scale From Grade1-4 as mild,moderates,evere and Potentially life-threatening. Higher the grade, more severe the symptoms. 1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, this participant was removed from overall safety population and presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[29]	371[30]		
Units: Participants				
ALT, Grade 1	24	18		
ALT, Grade 2	6	4		
ALT, Grade 3	1	1		
ALT, Grade 4	0	0		
Albumin, Grade 1	1	0		
Albumin, Grade 2	0	0		
Albumin, Grade 3	0	0		
Albumin, Grade 4	0	0		
ALP, Grade 1	2	0		
ALP, Grade 2	0	0		
ALP, Grade 3	0	0		
ALP, Grade 4	0	0		
AST, Grade 1	21	29		
AST, Grade 2	7	4		
AST, Grade 3	1	0		
AST, Grade 4	1	0		
Bilirubin, Grade 1	17	7		

Bilirubin, Grade 2	5	2		
Bilirubin, Grade 3	1	1		
Bilirubin, Grade 4	0	0		
CO2, Grade 1	73	70		
CO2, Grade 2	1	1		
CO2, Grade 3	0	0		
CO2, Grade 4	0	0		
Cholesterol, Grade 1	27	52		
Cholesterol, Grade 2	12	19		
Cholesterol, Grade 3	1	0		
Cholesterol, Grade 4	0	0		
CK, Grade 1	28	19		
CK, Grade 2	4	9		
CK, Grade 3	9	8		
CK, Grade 4	6	5		
Creatinine, Grade 1	16	7		
Creatinine, Grade 2	3	1		
Creatinine, Grade 3	0	0		
Creatinine, Grade 4	0	0		
Direct bilirubin, Grade 1	0	0		
Direct bilirubin, Grade 2	0	0		
Direct bilirubin, Grade 3	8	1		
Direct bilirubin, Grade 4	0	0		
GFR from creatinine adjusted using CKD EPI,Grade 1	0	0		
GFR from creatinine adjusted using CKD EPI,Grade 2	135	83		
GFR from creatinine adjusted using CKD EPI,Grade 3	26	13		
GFR from creatinine adjusted using CKD EPI,Grade 4	0	0		
GFR from cystatin C adjusted using CKD-EPI,Grade 1	0	0		
GFR from cystatin C adjusted using CKD-EPI,Grade 2	52	66		
GFR from cystatin C adjusted using CKD-EPI,Grade 3	5	4		
GFR from cystatin C adjusted using CKD-EPI,Grade 4	1	0		
Hypercalcemia, Grade 1	7	3		
Hypercalcemia, Grade 2	0	0		
Hypercalcemia, Grade 3	0	0		
Hypercalcemia, Grade 4	0	0		
Hyperglycemia, Grade 1	56	64		
Hyperglycemia, Grade 2	21	19		
Hyperglycemia, Grade 3	2	2		
Hyperglycemia, Grade 4	0	0		
Hyperkalemia, Grade 1	0	2		
Hyperkalemia, Grade 2	2	0		
Hyperkalemia, Grade 3	0	0		
Hyperkalemia, Grade 4	0	0		
Hypernatremia, Grade 1	1	1		
Hypernatremia, Grade 2	0	0		
Hypernatremia, Grade 3	0	0		

Hypernatremia, Grade 4	0	0		
Hypocalcemia, Grade 1	8	1		
Hypocalcemia, Grade 2	0	1		
Hypocalcemia, Grade 3	0	0		
Hypocalcemia, Grade 4	0	0		
Hypoglycemia, Grade 1	5	6		
Hypoglycemia, Grade 2	3	2		
Hypoglycemia, Grade 3	0	0		
Hypoglycemia, Grade 4	0	0		
Hypokalemia, Grade 1	7	1		
Hypokalemia, Grade 2	1	0		
Hypokalemia, Grade 3	0	0		
Hypokalemia, Grade 4	0	0		
Hyponatremia, Grade 1	8	13		
Hyponatremia, Grade 2	0	2		
Hyponatremia, Grade 3	0	0		
Hyponatremia, Grade 4	0	0		
LDL cholesterol, Grade 1	28	35		
LDL cholesterol, Grade 2	13	15		
LDL cholesterol, Grade 3	6	3		
LDL cholesterol, Grade 4	0	0		
Phosphate, Grade 1	38	47		
Phosphate, Grade 2	2	7		
Phosphate, Grade 3	0	0		
Phosphate, Grade 4	0	0		
Triglycerides, Grade 1	34	48		
Triglycerides, Grade 2	4	11		
Triglycerides, Grade 3	4	4		
Triglycerides, Grade 4	4	0		

Notes:

[29] - Safety Population.

[30] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants randomized to TBR arm receiving TDF-based regimen with Maximum Post-Baseline emergent clinical chemistry toxicities

End point title	Number of participants randomized to TBR arm receiving TDF-based regimen with Maximum Post-Baseline emergent clinical chemistry toxicities

End point description:

Blood samples were collected up to Week 36 visit for analysis of clinical chemistry parameters: ALT, albumin, ALP, AST, bilirubin, CO2, cholesterol, CK, creatinine, direct bilirubin, GFR from creatinine adjusted for BSA, GFR from cystatin C adjusted using CKD-EPI, hypercalcemia, hyperglycemia, hyperkalemia, hypernatremia, hypocalcemia, hypoglycemia, hypokalemia, hyponatremia, LDL cholesterol, phosphate and triglycerides. Any abnormality in clinical chemistry parameters were evaluated according to DAIDS toxicity scale From Grade 1 to 4: Grade 1 (mild), Grade 2 (moderate), Grade 3 (severe) and Grade 4 (Potentially life-threatening). Higher the grade, more severe the symptoms. One participant randomized to TBR but received TDF-based regimen and because safety profiles of TDF and TAF differ, this participant was removed from overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:
Up to Week 36

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[31]			
Units: Participants				
ALT, Grade 1	0			
ALT, Grade 2	0			
ALT, Grade 3	0			
ALT, Grade 4	0			
Albumin, Grade 1	0			
Albumin, Grade 2	0			
Albumin, Grade 3	0			
Albumin, Grade 4	0			
ALP, Grade 1	0			
ALP, Grade 2	0			
ALP, Grade 3	0			
ALP, Grade 4	0			
AST, Grade 1	0			
AST, Grade 2	0			
AST, Grade 3	0			
AST, Grade 4	0			
Bilirubin, Grade 1	0			
Bilirubin, Grade 2	0			
Bilirubin, Grade 3	0			
Bilirubin, Grade 4	0			
CO2, Grade 1	0			
CO2, Grade 2	0			
CO2, Grade 3	0			
CO2, Grade 4	0			
Cholesterol, Grade 1	0			
Cholesterol, Grade 2	0			
Cholesterol, Grade 3	0			
Cholesterol, Grade 4	0			
CK, Grade 1	0			
CK, Grade 2	0			
CK, Grade 3	0			
CK, Grade 4	0			
Creatinine, Grade 1	0			
Creatinine, Grade 2	0			
Creatinine, Grade 3	0			
Creatinine, Grade 4	0			
Direct bilirubin, Grade 1	0			
Direct bilirubin, Grade 2	0			
Direct bilirubin, Grade 3	0			
Direct bilirubin, Grade 4	0			

GFR from creatinine adjusted using CKD EPI,Grade 1	0			
GFR from creatinine adjusted using CKD EPI,Grade 2	0			
GFR from creatinine adjusted using CKD EPI,Grade 3	0			
GFR from creatinine adjusted using CKD EPI,Grade 4	0			
GFR from cystatin C adjusted using CKD-EPI,Grade 1	0			
GFR from cystatin C adjusted using CKD-EPI,Grade 2	0			
GFR from cystatin C adjusted using CKD-EPI,Grade 3	0			
GFR from cystatin C adjusted using CKD-EPI,Grade 4	0			
Hypercalcemia, Grade 1	0			
Hypercalcemia, Grade 2	0			
Hypercalcemia, Grade 3	0			
Hypercalcemia, Grade 4	0			
Hyperglycemia, Grade 1	0			
Hyperglycemia, Grade 2	0			
Hyperglycemia, Grade 3	0			
Hyperglycemia, Grade 4	0			
Hyperkalemia, Grade 1	0			
Hyperkalemia, Grade 2	0			
Hyperkalemia, Grade 3	0			
Hyperkalemia, Grade 4	0			
Hypernatremia, Grade 1	0			
Hypernatremia, Grade 2	0			
Hypernatremia, Grade 3	0			
Hypernatremia, Grade 4	0			
Hypocalcemia, Grade 1	0			
Hypocalcemia, Grade 2	0			
Hypocalcemia, Grade 3	0			
Hypocalcemia, Grade 4	0			
Hypoglycemia, Grade 1	0			
Hypoglycemia, Grade 2	0			
Hypoglycemia, Grade 3	0			
Hypoglycemia, Grade 4	0			
Hypokalemia, Grade 1	0			
Hypokalemia, Grade 2	0			
Hypokalemia, Grade 3	0			
Hypokalemia, Grade 4	0			
Hyponatremia, Grade 1	0			
Hyponatremia, Grade 2	0			
Hyponatremia, Grade 3	0			
Hyponatremia, Grade 4	0			
LDL cholesterol, Grade 1	0			
LDL cholesterol, Grade 2	0			
LDL cholesterol, Grade 3	0			
LDL cholesterol, Grade 4	0			
Phosphate, Grade 1	0			
Phosphate, Grade 2	0			

Phosphate, Grade 3	0			
Phosphate, Grade 4	0			
Triglycerides, Grade 1	1			
Triglycerides, Grade 2	0			
Triglycerides, Grade 3	0			
Triglycerides, Grade 4	0			

Notes:

[31] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in renal biomarkers- Urine albumin/creatinine (UA/C) ratio and Urine protein/creatinine (UP/C) ratio at Weeks 24 and 48

End point title	Change from Baseline in renal biomarkers- Urine albumin/creatinine (UA/C) ratio and Urine protein/creatinine (UP/C) ratio at Weeks 24 and 48

End point description:

Baseline is defined as Day 1. Change from Baseline in UA/C was calculated as UA/C ratio at post-Baseline visit minus UA/C ratio calculated at Baseline. Change from Baseline in UP/C and UA/C was calculated as UP/C and UA/C ratio at post-Baseline visit minus UP/C and UA/C ratio calculated at Baseline, respectively. Estimated geometric mean adjusted ratio and 95% CI have been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen. Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Participants with data available at specified data points were analyzed (represented by n= X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[32]	371[33]		
Units: Ratio				
geometric mean (confidence interval 95%)				
UA/C, Week 24, n=235, 230	1.080 (1.007 to 1.158)	1.022 (0.956 to 1.091)		
UA/C, Week 48, n=230, 224	1.125 (1.036 to 1.222)	1.059 (0.963 to 1.165)		
UP/C, Week 24, n=267, 261	0.955 (0.917 to 0.995)	0.976 (0.937 to 1.016)		
UP/C, Week 48, n=261, 257	0.971 (0.926 to 1.018)	1.016 (0.964 to 1.070)		

Notes:

[32] - Safety Population.

[33] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for UA/C at Week 24 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.257
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	1.057
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.164

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for UA/C at Week 48 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.35
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	1.062
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.936
upper limit	1.205

Statistical analysis title	Statistical Analysis 3
Statistical analysis description: Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for UP/C at Week 24 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.473
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	0.979

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.924
upper limit	1.037

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for UP/C at Week 48 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.212
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	0.956
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.891
upper limit	1.026

Secondary: Change from Baseline in renal biomarkers- UA/C ratio and UP/C ratio at Weeks 24 and 48 in participants randomized to TBR receiving TDF-based regimen

End point title	Change from Baseline in renal biomarkers- UA/C ratio and UP/C ratio at Weeks 24 and 48 in participants randomized to TBR receiving TDF-based regimen

End point description:

Urine samples were collected at Baseline, Week 24 and Week 48 to assess renal biomarkers - urine albumin/creatinine ratio and urine protein/creatinine ratio. Baseline was defined as the latest pre-dose assessment value (Day 1) with a non-missing value. Change from Baseline in UP/C and UA/C was calculated as UP/C and UA/C ratio at post-Baseline visit minus UP/C and UA/C ratio calculated at Baseline, respectively. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[34]			
Units: Ratio				
number (not applicable)				
UA/C, Week 24, n=1	0			
UA/C, Week 48, n=0	99999			
UP/C, Week 24, n=1	0.3			
UP/C, Week 48, n=0	99999			

Notes:

[34] - Safety Population. 99999 indicates no participant has been analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to Baseline in renal biomarkers- Urine beta-2 microglobulin/urine creatinine

End point title	Ratio to Baseline in renal biomarkers- Urine beta-2 microglobulin/urine creatinine

End point description:

Geometric mean ratio (visit/Baseline) and 95% CI of geometric mean ratio has been presented. Baseline was defined as Day 1. Change from Baseline in urine beta-2-microglobulin/urine creatinine was calculated as urine beta-2-microglobulin/urine creatinine ratio at post-Baseline visit minus urine beta-2-microglobulin/urine creatinine ratio calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Only those participants with data available at specified data points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[35]	371[36]		
Units: Ratio				
geometric mean (confidence interval 95%)				
Week 24, n=136, 141	0.991 (0.899 to 1.093)	1.034 (0.931 to 1.149)		
Week 48, n=126, 141	0.973 (0.870 to 1.088)	0.922 (0.832 to 1.022)		

Notes:

[35] - Safety Population.

[36] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine beta-2 microglobulin/urine creatinine at Week 24 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.56
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	0.958
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.106

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine beta-2 microglobulin/urine creatinine at Week 48 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.489
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	1.055
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.906
upper limit	1.229

Secondary: Change from Baseline in renal biomarkers- Urine beta-2 microglobulin/urine creatinine ratio in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarkers- Urine beta-2 microglobulin/urine creatinine ratio in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Urine biomarker samples were collected to assess urine beta-2 microglobulin/urine creatinine. Baseline (Day 1) value was the value from the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline in urine beta-2-microglobulin/urine creatinine was calculated as urine beta-2-microglobulin/urine creatinine ratio at post-Baseline visit minus urine beta-2-

microglobulin/urine creatinine ratio calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at weeks 24 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[37]			
Units: Ratio				
Week 24	99999			
Week 48	99999			

Notes:

[37] - Safety Population. 99999 indicates data was not collected for this outcome for this arm.

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to Baseline in renal biomarkers- Urine phosphate

End point title	Ratio to Baseline in renal biomarkers- Urine phosphate

End point description:

Urine biomarker samples were collected at Baseline and at Weeks 24 and 48 to assess urine phosphate. Geometric mean ratio (visit divided by Baseline) and 95% CI of geometric mean ratio has been presented. Baseline was defined as Day 1. Change from Baseline in urine phosphate was calculated as urine phosphate at post-Baseline visit minus urine phosphate calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Only those participants with data available at the specified data 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 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[38]	371[39]		
Units: Ratio				
geometric mean (confidence interval 95%)				
Week 24, n=348, 352	0.955 (0.888 to 1.028)	0.940 (0.871 to 1.014)		

Week 48, n=342, 340	0.969 (0.892 to 1.052)	0.970 (0.900 to 1.044)		

Notes:

[38] - Safety Population.

[39] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine phosphate at Week 48 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.985
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	0.999
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.894
upper limit	1.116

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine phosphate at Week 24 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.758
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	1.017
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.915
upper limit	1.13

Secondary: Change from Baseline in renal biomarkers- Urine phosphate in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarkers- Urine phosphate in

	participants randomized to TBR arm receiving TDF-based regimen

End point description:

Urine biomarker samples were collected to assess urine phosphate. Baseline (Day 1) value was the value from the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline in urine phosphate was calculated as urine phosphate at post-Baseline visit minus urine phosphate calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[40]			
Units: Ratio				
number (not applicable)				
Week 24, n=1	2.9			
Week 48, n=0	99999			

Notes:

[40] - Safety Population. 99999 indicates no participant has been analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Ratio to Baseline in renal biomarkers- Urine retinol binding protein 4/urine creatinine

End point title	Ratio to Baseline in renal biomarkers- Urine retinol binding protein 4/urine creatinine

End point description:

Geometric mean ratio (visit/Baseline) and 95% CI of geometric mean ratio has been presented. Baseline is defined as Day 1. Change from Baseline in Urine retinol binding protein 4/urine creatinine ratio was calculated as Urine retinol binding protein 4/urine creatinine ratio at post-Baseline visit minus Urine retinol binding protein 4/urine creatinine ratio calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Only those participants with data available at specified data points were analyzed (represented by n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[41]	371[42]		
Units: Ratio				
geometric mean (confidence interval 95%)				
Week 24, n=344, 343	0.860 (0.790 to 0.936)	0.920 (0.847 to 0.999)		
Week 48, n=340, 335	1.063 (0.992 to 1.139)	1.068 (0.996 to 1.144)		

Notes:

[41] - Safety Population.

[42] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine retinol binding protein 4/urine creatinine at Week 48 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.932
Method	Mixed Model Repeated Measures
Parameter estimate	Treatment ratio
Point estimate	0.996
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.903
upper limit	1.098

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine retinol binding protein 4/urine creatinine at Week 24 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.264
Method	Mixed Model Reported Measures
Parameter estimate	Treatment ratio
Point estimate	0.935

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.052

Secondary: Change from Baseline in renal biomarkers- Urine retinol binding protein 4/urine creatinine in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarkers- Urine retinol binding protein 4/urine creatinine in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Urine samples were collected to assess urine retinol binding protein 4/urine creatinine. Baseline was defined as Day 1. Change from Baseline in urine retinol binding protein 4/urine creatinine was calculated as urine retinol binding protein 4/urine creatinine ratio at post-Baseline visit minus urine retinol binding protein 4/urine creatinine ratio calculated at Baseline. One participant randomized to TBR but received TDF-based regimen and because safety profiles of TDF and TAF differ, this participant was removed from overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Treatment ratio (DTG+3TC/ TAF based regimen) and 95% CI for Urine retinol binding protein 4/urine creatinine at Week 48 has been presented. Participants with data available at specified data points were analyzed (represented by n= X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at weeks 24 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[43]			
Units: Ratio				
number (not applicable)				
Week 24, n=1	1.04			
Week 48, n=0	99999			

Notes:

[43] - Safety Population. 99999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipids at Weeks 24 and 48

End point title	Change from Baseline in fasting lipids at Weeks 24 and 48

End point description:

Blood samples were collected at Baseline (Day 1), Week 24 and Week 48 to assess fasting lipids which included plasma cholesterol, plasma LDL cholesterol, plasma high density lipoprotein (HDL) cholesterol and plasma triglycerides. Baseline value was the value from the latest pre-dose assessment (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. One participant randomized to TBR but received TDF-based regimen and because the safety

profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Only those participants with data available at the specified data 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 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[44]	371[45]		
Units: Millimoles per liter				
median (inter-quartile range (Q1-Q3))				
Plasma cholesterol, Week 24, n=282, 264	-0.325 (-0.750 to 0.150)	0.000 (-0.400 to 0.400)		
Plasma cholesterol, Week 48, n=275, 263	-0.200 (-0.750 to 0.150)	0.100 (-0.350 to 0.500)		
Plasma LDL Cholesterol, Week 24, n=282, 264	-0.210 (-0.570 to 0.130)	-0.060 (-0.340 to 0.410)		
Plasma LDL Cholesterol, Week 48, n=275, 263	-0.170 (-0.560 to 0.210)	0.070 (-0.320 to 0.430)		
Plasma Triglycerides, Week 24, n=282, 264	-0.100 (-0.460 to 0.160)	0.060 (-0.200 to 0.350)		
Plasma Triglycerides, Week 48, n=275, 263	-0.100 (-0.440 to 0.160)	0.100 (-0.280 to 0.380)		
Plasma HDL Cholesterol, Week 24, n=282, 264	-0.050 (-0.150 to 0.100)	0.050 (-0.150 to 0.150)		
Plasma HDL Cholesterol, Week 48, n=275, 263	0.000 (-0.200 to 0.150)	0.050 (-0.150 to 0.150)		

Notes:

[44] - Safety Population.

[45] - Safety Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipids at Weeks 24 and 48 in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in fasting lipids at Weeks 24 and 48 in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Blood samples were collected up to the Week 48 visit (participant withdrew from the study at Week 36) to assess fasting lipids which included plasma cholesterol, plasma LDL cholesterol, plasma HDL cholesterol and plasma triglycerides. Baseline value was the value from the latest pre-dose assessment (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. Change from Baseline values for fasting lipids in TDF-based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[46]			
Units: Millimoles per liter				
number (not applicable)				
Plasma cholesterol, Week 24, n=1	0			
Plasma cholesterol, Week 48, n=0	99999			
Plasma LDL Cholesterol, Week 24, n=1	-0.67			
Plasma LDL Cholesterol, Week 48, n=0	99999			
Plasma Triglycerides, Week 24, n=1	1.36			
Plasma Triglycerides, Week 48, n=0	99999			
Plasma HDL Cholesterol, Week 24, n=1	0.05			
Plasma HDL Cholesterol, Week 48, n=0	99999			

Notes:

[46] - Safety Population. 9999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with genotypic resistance

End point title	Number of participants with genotypic resistance

End point description:

Plasma samples were collected for drug resistance testing. Number of participants, who met confirmed virologic withdrawal (CVW) criteria (one plasma HIV-1 RNA >=200 c/mL after Day 1 with immediate prior HIV RNA >=50 c/mL), with emergent genotypic resistance to INSTI, nucleoside reverse transcriptase inhibitor (NRTI), NNRTI and PI was summarized. CVW Population comprises all participants in the ITT-E Population who had met the derived CVW criteria. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[47]	1[48]		
Units: Participants				
INSTI		0		
NRTI		0		
NNRTI		0		

PI		0		

Notes:

[47] - CVW Population.

[48] - CVW Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with phenotypic resistance

End point title	Number of participants with phenotypic resistance

End point description:

Number of participants, who meet CVW criteria (one plasma HIV-1 RNA >=200 c/mL after Day 1 with immediate prior HIV RNA >=50 c/mL), with emergent phenotypic resistance to INSTI and/or NRTI were summarized. Assessment of antiviral activity of anti-retroviral therapy (ART) using phenotypic test results was interpreted through a proprietary algorithm (from Monogram Biosciences), which provided the overall susceptibility of the drug. Partially sensitive and resistant calls were considered resistant in this analysis. The phenotypic resistance was calculated using binary scoring system, where 0 was considered as sensitive and 1 as resistance. Phenotypic Resistance data for the following INSTI, NNRTI, NRTI and PI drugs in participants Meeting CVW Criteria has been presented. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[49]	1[50]		
Units: Participants				
INSTI, DTG, Sensitive		1		
INSTI, DTG, Resistant		0		
INSTI, Bictegravir (BIC), Sensitive		1		
INSTI, BIC, Resistant		0		
INSTI, Elvitegravir (EVG), Sensitive		1		
INSTI, EVG, Resistant		0		
INSTI, Raltegravir (RAL), Sensitive		1		
INSTI, RAL, Resistant		0		
NNRTI, Delavirdine (DLV), Sensitive		1		
NNRTI, DLV, Resistant		0		
NNRTI, Efavirenz (EFV), Sensitive		1		
NNRTI, EFV, Resistant		0		
NNRTI, Etravirine (ETR), Sensitive		1		
NNRTI, ETR, Resistant		0		
NNRTI, Nevirapine (NVP), Sensitive		1		
NNRTI, NVP, Resistant		0		
NNRTI, Rilpivirine (RPV), Sensitive		1		
NNRTI, RPV, Resistant		0		
NRTI, 3TC, Sensitive		1		

NRTI, 3TC, Resistant		0		
NRTI, Abacavir (ABC), Sensitive		1		
NRTI, ABC, Resistant		0		
NRTI, Zidovudine (AZT), Sensitive		1		
NRTI, AZT, Resistant		0		
NRTI, Stavudine (D4T), Sensitive		1		
NRTI, D4T, Resistant		0		
NRTI, Didanosine (DDI), Sensitive		1		
NRTI, DDI, Resistant		0		
NRTI, Emtricitabine (FTC), Sensitive		1		
NRTI, FTC, Resistant		0		
NRTI, Tenofovir (TDF), Sensitive		1		
NRTI, TDF, Resistant		0		
PI, Atazanavir (ATV), Sensitive		1		
PI, ATV, Resistant		0		
PI, Darunavir (DRV), Sensitive		1		
PI, DRV, Resistant		0		
PI, Fosamprenavir (FPV), Sensitive		1		
PI, FPV, Resistant		0		
PI, Indinavir (IDV), Sensitive		1		
PI, IDV, Resistant		0		
PI, Lopinavir (LPV), Sensitive		1		
PI, LPV, Resistant		0		
PI, Nelfinavir (NFV), Sensitive		1		
PI, NFV, Resistant		0		
PI, Ritonavir (RTV), Sensitive		1		
PI, RTV, Resistant		0		
PI, Saquinavir (SQV), Sensitive		1		
PI, SQV, Resistant		0		
PI, Tipranavir (TPV), Sensitive		1		
PI, TPV, Resistant		0		

Notes:

[49] - CVW Population.

[50] - CVW Population.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone biomarkers-serum bone-specific ALP (Bone-ALP), osteocalcin, serum procollagen 1 N-Terminal propeptide (P1NP) and serum type 1 collagen C-telopeptides (CTX-1)

End point title	Change from Baseline in bone biomarkers-serum bone-specific ALP (Bone-ALP), osteocalcin, serum procollagen 1 N-Terminal propeptide (P1NP) and serum type 1 collagen C-telopeptides (CTX-1)

End point description:

Change from Baseline is post-dose visit value - Baseline value.Adjusted mean was estimated mean change from Baseline at each visit calculated from a repeated measures model adjusting for treatment, visit,Baseline third agent class, CD4+ cell count(continuous),age(continuous), sex, race, body mass index(BMI,continuous),smoking status, vitaminD use, Baseline biomarker(continuous),treatment by visit interaction, and Baseline value by visit interaction,with visit as repeated factor.1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, participant was removed from overall safety population and presented in separate arm"Randomized to TBR but received TDF-based regimen."Total of 741 participants were analyzed but 740 participants are presented in this

Outcome Measure and 1 participant is presented separately in next Outcome Measure. Participants with data available at specified data points were analyzed(n=X in category titles)

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[51]	371[52]		
Units: Micrograms per liter				
arithmetic mean (standard error)				
Bone-ALP, Week 24, n=350, 354	-0.77 (± 0.112)	-1.05 (± 0.089)		
Bone-ALP, Week 48, n=343, 342	-0.03 (± 0.145)	-0.34 (± 0.117)		
Osteocalcin, Week 24, n=350 ,353	-1.08 (± 0.248)	0.26 (± 0.229)		
Osteocalcin, Week 48, n=343, 342	-1.15 (± 0.260)	0.69 (± 0.279)		
P1NP, Week24, n=349 ,356	7.0 (± 0.87)	5.0 (± 0.72)		
P1NP, Week48, n=342, 343	9.3 (± 1.06)	6.4 (± 1.00)		
CTX-1, Week 24,n=350,356	0.0350 (± 0.01057)	-0.0031 (± 0.00833)		
CTX-1, Week 48, n=343, 343	0.0602 (± 0.01024)	0.0310 (± 0.00889)		

Notes:

[51] - Safety Population.

[52] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for Bone-ALP at Week 24 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.047
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.57

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for Bone-ALP at Week 48 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.094
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.68

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for Osteocalcin at Week 24 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.01
upper limit	-0.68

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for Osteocalcin at Week 48 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen

Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.59
upper limit	-1.09

Statistical analysis title	Statistical Analysis 5
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for P1NP at Week 24 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.066
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	2.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	4.3

Statistical analysis title	Statistical Analysis 6
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for P1NP at Week 48 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.046
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	2.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	5.8

Statistical analysis title	Statistical Analysis 7
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for CTX-1 at Week 24 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.0381
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0117
upper limit	0.0646

Statistical analysis title	Statistical Analysis 8
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for CTX-1 at Week 48 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.032
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.0292
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.0025
upper limit	0.0559

Secondary: Change from Baseline in bone biomarkers-serum bone-specific ALP (Bone-ALP), osteocalcin, serum P1NP and serum CTX-1 in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in bone biomarkers-serum bone-specific ALP (Bone-ALP), osteocalcin, serum P1NP and serum CTX-1 in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Serum samples were collected for analysis of bone biomarkers. Baseline was latest pre-dose assessment (Day 1) with a non-missing value. Change from Baseline is post-dose visit value minus Baseline value. Change from Baseline in bone biomarkers-serum bone-specific ALP (Bone-ALP), osteocalcin, serum P1NP and serum CTX-1 in TDF-based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[53]			
Units: Micrograms per liter				
number (not applicable)				
Bone-ALP, Week 24, n=1	0.3			
Bone-ALP, Week 48, n=0	99999			
Osteocalcin, Week 24, n=1	13.4			
Osteocalcin, Week 48, n=0	99999			
P1NP, Week24, n=1	11			
P1NP, Week48, n=0	99999			
CTX-1, Week 24,n=1	0.045			
CTX-1, Week 48, n=0	99999			

Notes:

[53] - Safety Population. 99999 indicates no participant has been analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in bone biomarker: serum 25-hydroxyvitamin D

End point title	Change from Baseline in bone biomarker: serum 25-hydroxyvitamin D

End point description:

Change from Baseline is post-dose visit value minus Baseline value. Adjusted mean was estimated mean change from Baseline at each visit in each arm calculated from repeated measures model adjusting for treatment, visit, Baseline third agent class, CD4+ cell count(continuous), age(continuous), sex, race, BMI(continuous), smoking status, vitaminD use, Baseline biomarker(continuous), treatment by visit interaction, and Baseline value by visit interaction, with visit as repeated factor.1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, participant was removed from overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Participants with data available at specified data points were analyzed(n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[54]	371[55]		
Units: Nanomoles per liter				
arithmetic mean (standard error)				
Week 24, n=351, 355	0.0 (± 1.10)	2.1 (± 1.15)		
Week 48, n=344, 343	-5.8 (± 1.21)	-3.5 (± 1.13)		

Notes:

[54] - Safety Population.

[55] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum 25 hydroxyvitamin D at Week 24 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.173
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	1

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum 25 hydroxyvitamin D at Week 48 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.168
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-2.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	1

Secondary: Change from Baseline in bone biomarker: serum 25-hydroxyvitamin D in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in bone biomarker: serum 25-hydroxyvitamin D in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Serum samples were collected for the analysis of 25-hydroxyvitamin D. Baseline value was the value from latest pre-dose assessment (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. Change from Baseline values for serum 25-hydroxyvitamin D in TDF-based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[56]			
Units: Nanomoles per liter				
Week 24, n=1	2			
Week 48, n=0	99999			

Notes:

[56] - Safety Population. 99999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in renal biomarker- serum cystatin C

End point title	Change from Baseline in renal biomarker- serum cystatin C

End point description:

Change from Baseline is post-dose visit value - Baseline value.Adjusted mean was estimated mean change from Baseline at each visit in each arm calculated from repeated measures model adjusting for following:treatment, visit, Baseline third agent class,CD4+ cell count(continuous), age(continuous),sex,race,BMI(continuous),presence of diabetes mellitus, hypertension,Baseline biomarker(continuous), treatment by visit interaction, and Baseline value by visit interaction, with visit repeated factor.1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, participant was removed from overall safety population and presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740

presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Participants with data available at specified data points were analyzed(n=X in category titles)

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[57]	371[58]		
Units: Milligrams per liter				
arithmetic mean (standard error)				
Week 24, n=351, 357	-0.03 (± 0.005)	-0.02 (± 0.004)		
Week 48, n=344, 343	0.00 (± 0.006)	0.01 (± 0.005)		

Notes:

[57] - Safety Population.

[58] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum cystatin C at Week 48 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.061
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum cystatin C at Week 24 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen

Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.027
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0

Secondary: Change from Baseline in renal biomarker- serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI at Weeks 24 and 48

End point title	Change from Baseline in renal biomarker- serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI at Weeks 24 and 48

End point description:

Change from Baseline is post-dose visit value - Baseline value. Adjusted mean was estimated mean change from Baseline at each visit in each arm calculated from repeated measures model adjusting for treatment, visit,Baseline third agent class,CD4+ cell count(continuous), age(continuous), sex, race,BMI(continuous), presence of diabetes mellitus, hypertension, Baseline biomarker(continuous), treatment by visit interaction, and Baseline value by visit interaction, with visit as repeated factor. 1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, participant was removed from overall safety population and presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure.Participants with data available at specified data points were analyzed (n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[59]	371[60]		
Units: Milliliters/minute/1.73*meter square				
arithmetic mean (standard error)				
GFR from cystatin C CKD-EPI, Week 24, n=351, 357	3.2 (± 0.52)	1.5 (± 0.46)		
GFR from cystatin C CKD-EPI, Week 48, n=344, 343	0.1 (± 0.61)	-1.6 (± 0.59)		
GFR from creatinine CKD-EPI, Week 24, n=351, 359	-8.8 (± 0.48)	-3.8 (± 0.47)		
GFR from creatinine CKD-EPI, Week 48, n=344, 345	-7.7 (± 0.48)	-2.9 (± 0.48)		

Notes:

[59] - Safety Population.

[60] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum GFR from cystatin C adjusted using CKD-EPI at Week 24 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.012
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	3.1

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum GFR from cystatin C adjusted using CKD-EPI at Week 48 has been presented	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.059
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	3.3

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum GFR from creatinine	

adjusted using CKD-EPI at Week 24 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.3
upper limit	-3.7

Statistical analysis title	Statistical Analysis 4

Statistical analysis description:

Mean difference (DTG+3TC - TAF based regimen) and its 95% CI for serum GFR from creatinine adjusted using CKD-EPI at Week 48 has been presented

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	-3.4

Secondary: Change from Baseline in renal biomarker- serum cystatin C in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarker- serum cystatin C in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Serum samples were collected at Baseline, Week 24 and Week 48 to assess renal inflammation biomarker - cystatin C. Baseline was defined as the latest pre-dose assessment value (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. Change from Baseline values for serum cystatin -C biomarker in TDF based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen." Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[61]			
Units: Milligrams per liter				
Week 24, n=1	0			
Week 48, n=0	99999			

Notes:

[61] - Safety Population. 99999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in renal biomarker- serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI at Weeks 24 and 48 in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarker- serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI at Weeks 24 and 48 in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Serum samples were collected at Baseline, Week 24 and Week 48 to assess renal inflammation biomarkers - serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI. Baseline was defined as the latest pre-dose assessment value (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. Change from Baseline in serum GFR from cystatin C adjusted using CKD-EPI and serum GFR from creatinine adjusted using CKD-EPI in TDF-based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen.” Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[62]			
Units: Milliliters/minute/1.73*meter square				

GFR from cystatin C CKD-EPI, Week 24, n=1	0			
GFR from cystatin C CKD-EPI, Week 48, n=0	99999			
GFR from creatinine CKD-EPI, Week 24, n=1	4			
GFR from creatinine CKD-EPI, Week 48, n=0	99999			

Notes:

[62] - Safety Population. 99999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in renal biomarker- serum creatinine

End point title	Change from Baseline in renal biomarker- serum creatinine

End point description:

Change from Baseline is post-dose visit value - Baseline value. Adjusted mean was estimated mean change from Baseline at each visit in each arm calculated from repeated measures model adjusting for treatment, visit, Baseline third agent class, CD4+ cell count(continuous), age(continuous), sex, race, BMI(continuous), presence of diabetes mellitus, hypertension, Baseline biomarker(continuous), treatment by visit interaction,and Baseline value by visit interaction, with visit as repeated factor. 1 participant randomized to TBR but received TDF and because safety profiles of TDF and TAF differ, participant was removed from overall safety population and presented in separate arm "Randomized to TBR but received TDF-based regimen." Total of 741 participants were analyzed but 740 participants are presented in this Outcome Measure and 1 participant is presented separately in next Outcome Measure. Participants with data available at specified data points were analyzed(n=X in category titles).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	369[63]	371[64]		
Units: Micromoles per liter				
arithmetic mean (standard error)				
Week 24, n=351, 359	7.47 (± 0.466)	3.11 (± 0.495)		
Week 48, n=344, 345	6.67 (± 0.493)	2.18 (± 0.450)		

Notes:

[63] - Safety Population.

[64] - Safety Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Mean difference (DTG+3TC - TBR) and its 95% CI for serum creatinine at Week 24 has been presented.

Comparison groups	DTG+3TC FDC v TAF-based regimen

Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	4.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.03
upper limit	5.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Mean difference (DTG+3TC - TBR) and its 95% CI for serum creatinine at Week 48 has been presented.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	740
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	4.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.18
upper limit	5.81

Secondary: Change from Baseline in renal biomarker- serum creatinine in participants randomized to TBR arm receiving TDF-based regimen

End point title	Change from Baseline in renal biomarker- serum creatinine in participants randomized to TBR arm receiving TDF-based regimen

End point description:

Serum samples were collected at Baseline, Week 24 and Week 48 to assess renal inflammation biomarker - serum creatinine. Baseline was defined as the latest pre-dose assessment value (Day 1) with a non-missing value. Change from Baseline is defined as post-dose visit value minus Baseline value. Change from Baseline in serum creatinine in TDF-based regimen participants has been presented. One participant randomized to TBR but received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen.” Only those participants with data available at the specified data 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 and 48

End point values	Randomized to TBR but received TDF-based regimen			
Subject group type	Subject analysis set			
Number of subjects analysed	1[65]			
Units: Micromoles per liter				
number (not applicable)				
Week 24, n=1 Week 48, n=0	-8 99999			

Notes:

[65] - Safety Population. 99999 indicates no participant has been analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) utility score at Week 24 and 48

End point title	Change from Baseline in European Quality of Life-5 Dimensions-5 Levels (EQ-5D-5L) utility score at Week 24 and 48

End point description:

EQ-5D-5L questionnaire provides a profile of participant function and a global health state rating. Five-item measure has 1 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. Health state is defined by combining levels of answers from each of 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. One participant randomized to TBR but received TDF and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable. Only those participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[66]	370[67]		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 24 Week 48	0.0029 (± 0.00383) 0.0037 (± 0.00407)	0.0046 (± 0.00352) 0.0023 (± 0.00373)		

Notes:

[66] - ITT-E Population.

[67] - ITT-E Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Week 48. MMRM adjusted for following: Treatment, Visit, Baseline Third Agent Class, Baseline EQ-5D Utility (continuous), Treatment by Visit interaction, and Baseline EQ-5D Utility by Visit interaction, with Visit as the repeated factor.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	734
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.792
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	0.0015
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0094
upper limit	0.0123

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Week 24. MMRM adjusted for following: Treatment, Visit, Baseline Third Agent Class, Baseline EQ-5D Utility (continuous), Treatment by Visit interaction, and Baseline EQ-5D Utility by Visit interaction, with Visit as the repeated factor.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	734
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.741
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.0017
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0119
upper limit	0.0085

Secondary: Change from Baseline in EQ-5D-5L Thermometer scores at Week 24 and

48

End point title	Change from Baseline in EQ-5D-5L Thermometer scores at Week 24 and 48

End point description:

EEQ-5D-5L questionnaire provides a profile of participant function and a global health state rating. The five-item measure has one question assessing each of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression and 5 levels for each dimension including 1=no problems, 2=slight problems, 3=moderate problems, 4=severe problems and 5=extreme problems. EQ-5D-5L included EQ visual Analogue scale (EQ VAS) 'Thermometer' which provided Self-rated current health status. Score ranges from 0 (worst imaginable health state) to 100 (best imaginable health state). MMRM was run on the LOCF dataset. Baseline was the latest pre-dose assessment value (Day 1) and change from Baseline=post-dose value minus Baseline value. One participant randomized to TBR but received TDF-based regimen and was presented within the "TBR (TAF-based regimen) arm" as efficacy of TAF and TDF are comparable. Participants with data available at specified time points has been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	DTG+3TC FDC	TAF-based regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364[68]	369[69]		
Units: Scores on a scale				
arithmetic mean (standard error)				
Week 24	1.2 (± 0.49)	1.3 (± 0.44)		
Week 48	1.1 (± 0.52)	1.7 (± 0.43)		

Notes:

[68] - ITT-E Population.

[69] - ITT-E Population.

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 24. MMRM adjusted for following: Treatment, Visit, Baseline Third Agent Class, Baseline EQ-5D Thermometer (continuous), Treatment by Visit interaction, and Baseline EQ-5D Thermometer by Visit interaction, with Visit as the repeated factor.

Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.879
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.4
upper limit	1.2

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Week 48. MMRM adjusted for following: Treatment, Visit, Baseline Third Agent Class, Baseline EQ-5D Thermometer (continuous), Treatment by Visit interaction, and Baseline EQ-5D Thermometer by Visit interaction, with Visit as the repeated factor.	
Comparison groups	DTG+3TC FDC v TAF-based regimen
Number of subjects included in analysis	733
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.414
Method	Mixed Model Repeated Measures
Parameter estimate	Mean difference (net)
Point estimate	-0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Non-SAEs and SAEs were collected from start of the study treatment (Day 1) up to Week 48.

Adverse event reporting additional description:

Safety Population. One participant randomized to TBR received TDF-based regimen and because the safety profiles of TDF and TAF differ, this participant was removed from the overall safety population and is presented in separate arm "Randomized to TBR but received TDF-based regimen."

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	DTG + 3TC

Reporting group description:

Participants who were on a stable TBR and who had an HIV-1 ribonucleic acid (RNA) <50 copies per millilter (c/mL) at the time of screening, received fixed dose combination of DTG 50 milligrams (mg) + 3TC 300 mg once daily up to 48 weeks.

Reporting group title	Randomized to TBR but received TDF-based regimen

Reporting group description:

Participant randomized to TBR arm who had HIV-1 RNA <50 c/mL at the time of screening, received TDF-based regimen instead of TAF-based regimen in error. Participant continued to receive TDF-regimen up to the Week 48 visit (participant withdrew from the study at Week 36).

Reporting group title	TAF Based Regimen

Reporting group description:

Participants who were on a stable TBR and who had an HIV-1 RNA<50 c/mL at the time of screening, were continued to receive TBR up to 48 weeks.

Serious adverse events	DTG + 3TC	Randomized to TBR but received TDF-based regimen	TAF Based Regimen
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 369 (5.69%)	0 / 1 (0.00%)	16 / 371 (4.31%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			

subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to liver			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Penile squamous cell carcinoma			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Amniorrhoea			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			

subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian haematoma			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatitis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 369 (0.54%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Suicide attempt			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Femoral neck fracture			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gun shot wound			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Nervous system disorders			
Cerebral haematoma			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary dyskinesia			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteitis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 369 (0.54%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amniotic cavity infection			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Labyrinthitis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis pneumococcal			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pertussis			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shigella infection			
subjects affected / exposed	0 / 369 (0.00%)	0 / 1 (0.00%)	1 / 371 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 369 (0.27%)	0 / 1 (0.00%)	0 / 371 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	DTG + 3TC	Randomized to TBR but received TDF-based regimen	TAF Based Regimen
Total subjects affected by non-serious adverse events			
subjects affected / exposed	222 / 369 (60.16%)	1 / 1 (100.00%)	204 / 371 (54.99%)
Nervous system disorders			
Headache			
subjects affected / exposed	24 / 369 (6.50%)	0 / 1 (0.00%)	17 / 371 (4.58%)
occurrences (all)	37	0	19
Dizziness			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	8	0	8
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	20 / 369 (5.42%)	0 / 1 (0.00%)	3 / 371 (0.81%)
occurrences (all)	20	0	3
Immune system disorders			

Seasonal allergy			
subjects affected / exposed	12 / 369 (3.25%)	0 / 1 (0.00%)	3 / 371 (0.81%)
occurrences (all)	13	0	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	30 / 369 (8.13%)	1 / 1 (100.00%)	26 / 371 (7.01%)
occurrences (all)	34	1	28
Nausea			
subjects affected / exposed	15 / 369 (4.07%)	0 / 1 (0.00%)	7 / 371 (1.89%)
occurrences (all)	16	0	7
Abdominal pain			
subjects affected / exposed	9 / 369 (2.44%)	0 / 1 (0.00%)	7 / 371 (1.89%)
occurrences (all)	12	0	7
Toothache			
subjects affected / exposed	5 / 369 (1.36%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	5	0	9
Vomiting			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	4 / 371 (1.08%)
occurrences (all)	8	0	4
Constipation			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	2 / 371 (0.54%)
occurrences (all)	9	0	2
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	4 / 369 (1.08%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	4	0	8
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 369 (1.63%)	0 / 1 (0.00%)	9 / 371 (2.43%)
occurrences (all)	6	0	9
Psychiatric disorders			
Anxiety			
subjects affected / exposed	16 / 369 (4.34%)	0 / 1 (0.00%)	9 / 371 (2.43%)
occurrences (all)	16	0	10
Depression			

subjects affected / exposed	9 / 369 (2.44%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	9	0	8
Insomnia			
subjects affected / exposed	10 / 369 (2.71%)	0 / 1 (0.00%)	7 / 371 (1.89%)
occurrences (all)	10	0	7
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	21 / 369 (5.69%)	0 / 1 (0.00%)	28 / 371 (7.55%)
occurrences (all)	22	0	31
Arthralgia			
subjects affected / exposed	12 / 369 (3.25%)	0 / 1 (0.00%)	13 / 371 (3.50%)
occurrences (all)	12	0	13
Pain in extremity			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	4 / 371 (1.08%)
occurrences (all)	8	0	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	43 / 369 (11.65%)	0 / 1 (0.00%)	41 / 371 (11.05%)
occurrences (all)	53	0	51
Upper respiratory tract infection			
subjects affected / exposed	31 / 369 (8.40%)	1 / 1 (100.00%)	32 / 371 (8.63%)
occurrences (all)	42	1	38
Syphilis			
subjects affected / exposed	24 / 369 (6.50%)	0 / 1 (0.00%)	13 / 371 (3.50%)
occurrences (all)	25	0	13
Gastroenteritis			
subjects affected / exposed	13 / 369 (3.52%)	0 / 1 (0.00%)	16 / 371 (4.31%)
occurrences (all)	16	0	16
Bronchitis			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	20 / 371 (5.39%)
occurrences (all)	8	0	21
Pharyngitis			
subjects affected / exposed	14 / 369 (3.79%)	0 / 1 (0.00%)	11 / 371 (2.96%)
occurrences (all)	15	0	12
Anal chlamydia infection			

subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	12 / 371 (3.23%)
occurrences (all)	9	0	16
Influenza			
subjects affected / exposed	9 / 369 (2.44%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	9	0	8
Urinary tract infection			
subjects affected / exposed	6 / 369 (1.63%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	8	0	10
Urethritis			
subjects affected / exposed	9 / 369 (2.44%)	0 / 1 (0.00%)	4 / 371 (1.08%)
occurrences (all)	9	0	4
Proctitis gonococcal			
subjects affected / exposed	8 / 369 (2.17%)	0 / 1 (0.00%)	3 / 371 (0.81%)
occurrences (all)	9	0	5
Oral herpes			
subjects affected / exposed	3 / 369 (0.81%)	0 / 1 (0.00%)	8 / 371 (2.16%)
occurrences (all)	3	0	8
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	12 / 369 (3.25%)	0 / 1 (0.00%)	11 / 371 (2.96%)
occurrences (all)	12	0	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 May 2017	Amendment 01: TAF was corrected by removal of the word "fumarate". Clarification was provided in the overall design to specify that participants randomized to TBR will switch to DTG/3TC FDC at Week 52 if human immunodeficiency virus-1 ribonucleic acid (HIV-1 RNA) <50 copies per milliliter (c/mL) at Week 48 (or upon retest by Week 52). Biomarkers of inflammation and mitochondrial function were removed as exploratory endpoints. A Week 96 endpoint was added to the measurement of biomarkers of telomerase function in a subset of participants. Cardiovascular biomarker measurements were removed as exploratory endpoints. Inclusion Criteria #5 was edited for clarity. Protocol Section 6.2, Protocol Permitted Substitutions, added. The text defining the TBR comparators as investigational medicinal product was removed; TBR comparators are provided in designated, specific countries only, as needed. The Time and Events Table was modified to clarify that whole blood samples could be utilized for virology and for telomere length measurements, and cryopreserved peripheral blood mononuclear cells (PBMCs) could be used to evaluate telomerase activity. Updated version of Division of acquires immunodeficiency syndrome (AIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (version 2.1), March 2017, was provided in Protocol Section 12.9. Changes were made to the protocol text to reflect the addition of Country Specific requirements for Japan.
13 June 2017	Amendment 02: The impetus for this protocol amendment was to update Protocol Appendix 5, Protocol Appendix 6 and Protocol Appendix 8 based on the ViiV Healthcare templates for these appendices that were appropriate for the HIV participant population.
24 August 2017	Amendment 03: Amended to include: Addition of cluster of differentiation 8 plus (CD8+) lymphocyte assessments, addition of inflammatory biomarkers assessments as new exploratory endpoints, and revision of the sample size based on updated estimates for the primary endpoint for the investigational arm.
07 December 2017	Amendment 04: Amended to include pharmacokinetics assessments in the DTG/3TC FDC arm as exploratory endpoints; to update exclusion criterion 18 and remove its corresponding secondary endpoint no longer relevant; and to add glycated hemoglobin (HbA1c) and homeostasis model of assessment-insulin resistance (HOMA-IR) assessments. For clarification purposes, the adverse event (AE) severity grading in Protocol Appendix 8 and Protocol Section 13.8.6 (Evaluating AEs and serious adverse events [SAEs]) were updated to be consistent with Protocol Appendix 9, Protocol Section 13.9 (Division of AIDS table for Grading Severity of Adult and Pediatric Adverse Events). This change has no impact on the investigator's evaluation of adverse events. Text was edited in Protocol Appendix 10, Protocol Section 13.10.2 to clarify wording for the country specific requirement for Japan.

14 June 2018	Amendment 05: Changes were made to the protocol to manage and mitigate risks following identification of a potential safety issue related to neural tube defects in infants born to women with exposure to DTG at the time of conception. Changes were also made to include updated text to address a higher number of participants screened than planned, to update references to the DTG Investigator's Brochure (IB) to reflect the most current versions and to add clarification and correct minor typos. The Risk Assessment table (Protocol Section 4.6.1) was updated to include language regarding risk and mitigation of neural tube defects. The withdrawal criteria (Protocol Section 5.4) were updated to include a reminder that females of reproductive potential who change their minds and desire to be pregnant, or who state they no longer are willing to comply with the approved pregnancy avoidance methods, would also be withdrawn from the study. The Time and Events table (Protocol Section 7.1) was updated to include a reminder for investigators to check at every visit that females of reproductive potential are avoiding pregnancy. The modified list of highly effective methods for avoiding pregnancy in females of reproductive potential (FRP) (Protocol Section 13.3.1) was updated to exclude the double barrier method of contraception, which does not meet the updated GlaxoSmithKline [GSK]/ViiV criteria for a highly effective method. The Type and Number of participants (Protocol Section 4.3) and Sample Size Assumptions (Protocol Section 9.2.1) were updated to address a higher number of participants screened than planned.
29 August 2018	Amendment 06: Changes were made to the protocol to update the study design to extend the Randomized Early Switch Phase through to 148 weeks instead of Week 52, delaying the late switch to Week 148 with long-term follow-up through to completion of the study at Week 200. The rationale for this change was to collect and assess long-term comparative efficacy and safety data for DTG/3TC FDC vs. a TAF-based regimen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported