Clinical trial results:
A Phase III, randomized, multicenter, parallel-group, non inferiority study evaluating the efficacy, safety, and tolerability of switching to dolutegravir plus rilpivirine from current INSTI-, NNRTI-, or PI-based antiretroviral regimen in HIV-1-infected adults who are virologically suppressed.

Summary

EudraCT number	2014-005148-16
Trial protocol	ES DE GB FR IT
Global end of trial date	

Results information

Result version number	v3
This version publication date	11 November 2017
First version publication date	12 August 2017
Version creation reason	• Correction of full data set Add DEXA sub-study link

Trial information

Trial identification

Sponsor protocol code	201637

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	20 February 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 September 2016
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 dolutegravir (DTG) plus rilpivirine (RPV) once daily compared to continuation of current antiretroviral regimen (CAR) over 48 weeks in HIV-1 infected antiretroviral therapy (ART)-experienced virologically suppressed subjects.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 24
Country: Number of subjects enrolled	Australia: 34
Country: Number of subjects enrolled	Canada: 38
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Italy: 18
Country: Number of subjects enrolled	Russian Federation: 30
Country: Number of subjects enrolled	Spain: 245
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	United States: 40
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	518
EEA total number of subjects	335

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)	507
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was a 148-week, Phase III, randomized, open-label, active-controlled, multicenter, parallel-group, non-inferiority study to assess the antiviral activity and safety of a two-drug regimen of dolutegravir (DTG) + rilpivirine (RPV) compared with current antiretroviral regimen (CAR). The study was conducted in 60 centers in 11 countries.

Pre-assignment

Screening details:

Total 670 participants were screened (152 failed), 518 participants were randomized and 2 subjects withdrew before being exposed to study drug. The study included a Screening phase, an early switch phase, a late switch phase, and a continuation phase. The results presented are based on the interim analysis of the early phase.

Period 1

Period 1 title	52-Week early switch phase (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 + RPV

Arm description:

Participants received DTG 50 milligrams (mg) + RPV 25 mg together once daily at approximately the same time, with a meal, in an open-label fashion up to Week 52 during early switch phase.

Arm type	Experimental
Investigational medicinal product name	Rilpivirine Tablets 25 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received rilpivirine tablets 25 mg once daily, with a meal, in an open-label fashion up to Week 52 during early switch phase.

Investigational medicinal product name	Dolutegravir Tablets 50 mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received dolutegravir tablets 50 mg once daily, with a meal, in an open-label fashion up to Week 52 during early switch phase.

Arm title	Current antiretroviral regimen

Arm description:

Participants continued to receive their current antiretroviral regimen (two nucleoside reverse transcriptase inhibitors [NRTIs] + a third agent). A third agent included either an: integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI). CAR was administered according to the approved labeling in an open-label fashion up to Week 52 during early switch phase.

Arm type	Active comparator

Investigational medicinal product name	Current antiretroviral regimen (not IMP)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants received their current antiretroviral regimen (2 NRTIs + a third agent). A third agent included either of INSTI, NNRTI, or PI. CAR was administered according to the approved labeling in an open-label fashion up to Week 52 during early switch phase.

Number of subjects in period 1[1]	DTG + RPV	Current antiretroviral regimen
Started	261	255
Completed	245	239
Not completed	16	16
Adverse event, serious fatal	1	-
Consent withdrawn by subject	2	7
Physician decision	-	1
Adverse event, non-fatal	10	1
Subject reached stopping criteria	1	1
Lost to follow-up	1	1
Lack of efficacy	1	2
Protocol deviation	-	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: Total 670 subjects were screened, 518 were randomized and 2 subjects withdrew before being exposed to study drug.

Baseline characteristics

Reporting groups	
Reporting group title	DTG + RPV
Reporting group description:	
Participants received DTG 50 milligrams (mg) + RPV 25 mg together once daily at approximately the same time, with a meal, in an open-label fashion up to Week 52 during early switch phase.	
Reporting group title	Current antiretroviral regimen
Reporting group description:	
Participants continued to receive their current antiretroviral regimen (two nucleoside reverse transcriptase inhibitors [NRTIs] + a third agent). A third agent included either an: integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI). CAR was administered according to the approved labeling in an open-label fashion up to Week 52 during early switch phase.	

Reporting group values	DTG + RPV	Current antiretroviral regimen	Total
Number of subjects	261	255	516
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	43.3	43.2	
standard deviation	± 11.34	± 9.64	-
Gender categorical Units: Subjects			
Female	62	57	119
Male	199	198	397
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	11	8	19
Central/South Asian Heritage	0	1	1
Japanese/East Asian (EA) Heritage (H.)/South EA H.	13	15	28
Black/African American	13	20	33
Native Hawaiian or other Pacific Islander	1	0	1
White	223	210	433
African American/ African H. and White	0	1	1

End points

End points reporting groups

Reporting group title	DTG + RPV
Reporting group description:	
Participants received DTG 50 milligrams (mg) + RPV 25 mg together once daily at approximately the same time, with a meal, in an open-label fashion up to Week 52 during early switch phase.	
Reporting group title	Current antiretroviral regimen
Reporting group description:	
Participants continued to receive their current antiretroviral regimen (two nucleoside reverse transcriptase inhibitors [NRTIs] + a third agent). A third agent included either an: integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI). CAR was administered according to the approved labeling in an open-label fashion up to Week 52 during early switch phase.	
Subject analysis set title	dtg 50 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received DTG 50 mg + RPV 25 mg together once daily, with a meal, in an open-label fashion up to Week 52 during early switch phase.	
Subject analysis set title	rpv 25 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received DTG 50 mg +RPV 25 mg together once daily, with a meal, in an open-label fashion up to Week 52 during early switch phase.	

Primary: Percentage of participants with plasma human immunodeficiency virus (HIV) 1 ribonucleic acid (RNA) <50 copies/milliliter (c/mL) at Week 48 using snapshot algorithm

End point title	Percentage of participants with plasma human immunodeficiency virus (HIV) 1 ribonucleic acid (RNA) <50 copies/milliliter (c/mL) at Week 48 using snapshot algorithm
End point description:	
Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Week 48 using the Food and Drug Administration (FDA) snapshot algorithm was assessed to demonstrate the non-inferior antiviral activity of switching to DTG+RPV once daily compared to continuation of CAR over 48 weeks in HIV-1 infected antiretroviral therapy (ART)-experienced participants. Virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment within the window of the visit of interest. Plasma samples were collected for HIV-1 RNA at Week 0 (Day 1), Week 4, 8, 12, 24, 36 and 48. Treatment with DTG + RPV were declared non-inferior to CAR if the lower end of a two-sided 95% confidence interval for the difference between the two groups in response rates at Week 48 lies above -10% by Cochran-Mantel Haenszel test. The Intent-to-Treat Exposed (ITT-E) population consisted of all randomly assigned participants who received at least one dose of study drug.	
End point type	Primary
End point timeframe:	
Week 48.	

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[1]	255[2]		
Units: Percentage of participants				
Participants	94	94		

Notes:

[1] - ITT-E Population

[2] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Estimates based on Cochran-Mantel Haenszel stratified analysis adjusting for Baseline stratification factors: Age group (< or >=50 years old) and Baseline third agent (PI, NNRTI, INSTI).

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Risk difference (RD)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.9
upper limit	4.2

Notes:

[3] - Non-inferiority can be concluded if the lower bound of a two-sided 95% confidence interval for the difference in response rates between the two treatment arms is greater than -10%.

Secondary: Changes from Baseline in cluster designation (CD)4+ lymphocyte count at Weeks 24 and 48

End point title	Changes from Baseline in cluster designation (CD)4+ lymphocyte count at Weeks 24 and 48

End point description:

Blood was collected and CD4+ cell count assessment by flow cytometery was carried out at Baseline (Day 1), Week 4, 8, 12, 24, 36 and 48 to evaluate the immunological activity of DTG + RPV once daily compared to continuation of CAR. The full set of lymphocyte sub sets was not evaluated. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Week 24 and 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[4]	255[5]		
Units: Cells per millimeter (mm)^3				
arithmetic mean (standard deviation)				
Week 24, n=251, 250	42 (± 172.29)	42.4 (± 164.85)		

Week 48, n=245, 241	28 (± 169.35)	18.4 (± 159.34)		

Notes:

[4] - ITT-E Population

[5] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Week 24 using the FDA snapshot algorithm was assessed to evaluate the antiviral activity of DTG +RPV once daily compared to continuation of CAR. Virologic success or failure was determined by the last available HIV-1 RNA assessment while the participant was on-treatment within the window of the visit of interest. Plasma samples were collected for HIV-1 RNA at Baseline(Day 1), Week 4, 8, 12 and 24.

End point type	Secondary

End point timeframe:

Week 24

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[6]	255[7]		
Units: Percentage of participants				
Percentage of participants	97	98		

Notes:

[6] - ITT-E Population

[7] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Cochran-Mantel Haenszel stratified analysis adjusting for Baseline stratification factors: Age group (< or >=50 years old) and Baseline third agent (PI, NNRTI, INSTI). No formal non-inferiority margin has been pre-specified for secondary endpoints.

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-1.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	1.8

Secondary: Number of participants with common non-serious adverse event (AE), any serious AE (SAE), AE of maximum toxicity grade 1, 2, 3 or 4 and AE leading to discontinuation (AELD)

End point title	Number of participants with common non-serious adverse event (AE), any serious AE (SAE), AE of maximum toxicity grade 1, 2, 3 or 4 and AE leading to discontinuation (AELD)

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any untoward event resulting in death, life threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, congenital anomaly/birth defect, any other situation according to medical or scientific judgment that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention were categorized as SAE. Number of participants with common non-serious AE, SAE, drug related AE or SAE, AELD or AE with maximum grade toxicity was summarized. Common AEs were those with >5 percent incidence for either treatment. Safety Population included all randomly assigned participants who have received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Up to Week 52

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[8]	255[9]		
Units: Participants				
Common non-serious AE	61	59		
Any SAE	18	9		
Maximum toxicity Grade 1 AE	119	122		
Maximum toxicity Grade 2 AE	59	47		
Maximum toxicity Grade 3 AE	16	4		
Maximum toxicity Grade 4 AE	1	1		
AELD	12	1		

Notes:

[8] - Safety Population

[9] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-baseline emergent chemistry toxicities over 48 weeks

End point title	Number of participants with maximum post-baseline emergent

	chemistry toxicities over 48 weeks

End point description:

Blood samples were collected at Baseline (Day 1) and at Week 4, 8, 12, 24, 36 and 48 to evaluate alanine aminotransferase (ALT), albumin, alkaline phosphatase (ALP), aspartate aminotransferase (AST), total bilirubin, chloride, creatinine, glucose, potassium, phosphate, sodium, blood urea nitrogen (BUN), total carbon dioxide, lipase, creatine phosphokinase and creatinine clearance. Value obtained at Day 1 was considered as Baseline value. Change from Baseline was calculated as value at indicated time point minus Baseline value. Number of participants who experienced maximum grade toxicity post-baseline in clinical chemistry over 48 weeks was summarized. Participants were graded using the Division of AIDS Table for Grading Severity of Adult and Pediatric Adverse Events. Grade 1=mild; grade 2=moderate; grade 3=severe; grade 4=potentially life-threatening. For all laboratory parameters, one assessment out of range was sufficient to be considered a chemistry toxicity.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[10]	255[11]		
Units: Participants				
Grade 1	92	80		
Grade 2	72	79		
Grade 3	11	16		
Grade 4	1	10		

Notes:

[10] - Safety Population

[11] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-baseline emergent hematology toxicities over 48 weeks

End point title	Number of participants with maximum post-baseline emergent hematology toxicities over 48 weeks

End point description:

Blood samples were collected at Baseline (Day 1) and at Week 4, 8, 12, 24, 36 and 48 to evaluate hemoglobin, hematocrit, basophils, eosinophils, lymphocytes, monocytes, neutrophils, mean corpuscular volume (MCV), red blood cell (RBC) count, white blood cell (WBC) count and platelet count. Change from Baseline was calculated as value at indicated time point minus Baseline value. Number of participants who experienced maximum grade toxicity post-baseline in hematology over 48 weeks was summarized.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[12]	255[13]		
Units: Participants				
Grade 1	11	11		
Grade 2	2	2		
Grade 3	3	0		
Grade 4	1	0		

Notes:

[12] - Safety Population

[13] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in high-sensitivity C-reactive protein (hs-CRP) at Week 48

End point title	Mean change from Baseline in high-sensitivity C-reactive protein (hs-CRP) at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and 48 to assess hs-CRP. Change from Baseline was calculated as value at indicated time point minus Baseline value.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[14]	239[15]		
Units: mg/ Liter (L)				
arithmetic mean (standard deviation)				
mg/ Liter (L)	0.1 (± 5.383)	0.8 (± 8.527)		

Notes:

[14] - Safety Population

[15] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in cystatin C at Week 48

End point title	Mean change from Baseline in cystatin C at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess cystatin C. Change from Baseline was calculated as value at indicated time point minus Baseline value.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[16]	237[17]		
Units: mg/L				
arithmetic mean (standard deviation)				
mg/L	-0.02 (± 0.11)	-0.01 (± 0.108)		

Notes:

[16] - Safety Population

[17] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in D-Dimer at Week 48

End point title	Mean change from Baseline in D-Dimer at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess D-Dimer. Change from Baseline was calculated as value at indicated time point minus Baseline value.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[18]	228[19]		
Units: Nanomole (nmol)/L FEU				
arithmetic mean (standard deviation)				
Nanomole (nmol)/L FEU	0.01 (± 1.629)	-0.13 (± 2.932)		

Notes:

[18] - Safety Population

[19] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in fatty acid binding protein 2 (FABP) and soluble CD14 at Week 48

End point title	Mean change from Baseline in fatty acid binding protein 2

	(FABP) and soluble CD14 at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess FABP and soluble CD14. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[20]	255[21]		
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)				
FABP, n=245, 236	-1.5 (± 1.278)	-0.99 (± 1.441)		
Soluble CD14, n=245, 237	456.69 (± 731.833)	802.26 (± 878.304)		

Notes:

[20] - Safety Population

[21] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in Soluble CD163 and oxidized low density lipoprotein (LDL) at Week 48

End point title	Mean change from Baseline in Soluble CD163 and oxidized low density lipoprotein (LDL) at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess soluble CD163 and oxidized LDL. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[22]	255[23]		
Units: Microgram/Liter				
arithmetic mean (standard deviation)				
Soluble CD163, n=245, 236	65.38 (± 180.869)	53.94 (± 215.621)		

Oxidized LDL, n=245, 237	60.87 (± 504.345)	13.92 (± 575.305)		

Notes:

[22] - Safety Population

[23] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in retinol binding protein (RBP), serum creatinine and glucose at Week 48

End point title	Mean change from Baseline in retinol binding protein (RBP), serum creatinine and glucose at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess RBP, serum creatinine and glucose. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[24]	255[25]		
Units: mg/ deciliter (dL)				
arithmetic mean (standard deviation)				
RBP, n=245, 237	-0.13 (± 0.825)	0 (± 0.872)		
Serum creatinine, n=245, 241	0.1 (± 0.1053)	-0.003 (± 0.0847)		
Glucose, n=242, 235	0.187 (± 19.5808)	3.22 (± 10.0987)		

Notes:

[24] - Safety Population

[25] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in urine phosphate at Week 48

End point title	Mean change from Baseline in urine phosphate at Week 48

End point description:

Urine biomarker samples were collected to at Baseline (Day 1) and Week 48 to assess urine phosphate. Change from Baseline was calculated as value at indicated time point minus Baseline value.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	235[26]	229[27]		
Units: Millimoles (mmol)/ L				
arithmetic mean (standard deviation)				
Millimoles (mmol)/ L	1.335 (± 16.7211)	-0.798 (± 15.3771)		

Notes:

[26] - Safety Population

[27] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in beta-2-microglobulin (B2M) (blood and urine), urine RBP and 25 hydroxy-vitamin D at Week 48

End point title	Mean change from Baseline in beta-2-microglobulin (B2M) (blood and urine), urine RBP and 25 hydroxy-vitamin D at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess B2M and 25 hydroxy-vitamin D. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles). For 25 hydroxy-vitamin D, analysis of changes from Baseline was performed on log-transformed data. Results were transformed back via exponential transformation such that treatment comparisons are assessed via odds ratios.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[28]	255[29]		
Units: Nanomoles (nmol)/ L				
arithmetic mean (standard deviation)				
B2M, blood, n=245, 238	-16.88 (± 34.8933)	-4.7501 (± 43.04355)		
25 hydroxy-vitamin D, n=243, 239	-13.9 (± 25.3)	-9.2 (± 19.55)		
Urine B2M, n=72, 78	-173.282 (± 1311.24142)	62.3209 (± 391.32049)		
Urine RBP, n=232, 224	-6.8123 (± 24.0965)	-0.0631 (± 11.99886)		

Notes:

[28] - Safety Population

[29] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other[30]
P-value	= 0.007 [31]
Method	ANCOVA

Notes:

[30] - Since statistical significance at the 10% level was observed, results are presented separately per Baseline third agent.

[31] - P-value for interaction between treatment group and Baseline third agent (25 hydroxy-vitamin D)

Statistical analysis title	Statistical analysis 2
Statistical analysis description:	
Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.	
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.011 [32]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.861
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.767
upper limit	0.967

Notes:

[32] - P value to assess difference between treatment groups (25 hydroxy-vitamin D - INSTI)

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.	
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.745 [33]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.012

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.943
upper limit	1.085

Notes:

[33] - P value to assess difference between treatment groups (25 hydroxy-vitamin D - NNRTI)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.018 [34]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.877
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.787
upper limit	0.977

Notes:

[34] - P value to assess difference between treatment groups (25 hydroxy-vitamin D - PI)

Secondary: Mean change from Baseline in urine albumin/creatinine ratio and urine protein/creatinine ratio at Week 48

End point title	Mean change from Baseline in urine albumin/creatinine ratio and urine protein/creatinine ratio at Week 48

End point description:

Urine biomarker samples were collected at Baseline (Day 1) and Week 48 to assess urine albumin/creatinine ratio and urine protein/creatinine ratio. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[35]	255[36]		
Units: Grams (g)/ mol				
arithmetic mean (standard deviation)				
Urine albumin/creatinine ratio, n=178, 181	-0.78 (± 5.116)	-0.64 (± 9.538)		

Urine protein/creatinine ratio, n=192, 193	-2.73 (± 12.683)	1.23 (± 5.088)		

Notes:

[35] - Safety Population

[36] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in bone-specific alkaline phosphatase, procollagen 1 N-terminal propeptide, osteocalcin, Type 1 Collagen C-telopeptides and soluble vascular cell adhesion molecule (sVCAM) at Week 48

End point title	Mean change from Baseline in bone-specific alkaline phosphatase, procollagen 1 N-terminal propeptide, osteocalcin, Type 1 Collagen C-telopeptides and soluble vascular cell adhesion molecule (sVCAM) at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess bone-specific alkaline phosphatase, procollagen 1 N-terminal propeptide, osteocalcin, Type 1 Collagen C-telopeptides and sVCAM. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles). For bone-specific alkaline phosphatase, procollagen 1-N-propeptide, osteocalcin and type 1 collagen C-telopeptide, analyses of changes from Baseline were performed on log-transformed data. Results were transformed back via exponential transformation such that treatment comparisons are assessed via odds ratios.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[37]	255[38]		
Units: Microgram (ug)/ L				
arithmetic mean (standard deviation)				
Bone-specific alkaline phosphatase, n=246, 236	-3.18 (± 5.678)	0.92 (± 4.634)		
Procollagen type 1 N-propeptide, n=245, 237	-5.8 (± 20)	0.3 (± 19.28)		
Osteocalcin, n=245, 235	-5.11 (± 7.334)	-1.14 (± 6.017)		
Type I Collagen C-Telopeptides, n=243, 238	-0.15 (± 0.31)	-0.09 (± 0.344)		
sVCAM, n=245, 237	-2.63 (± 571.182)	37.42 (± 617.486)		

Notes:

[37] - Safety Population

[38] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other[39]
P-value	= 0.001 [40]
Method	ANCOVA

Notes:

[39] - Since statistical significance at the 10% level was observed, results are presented separately per Baseline third agent.
[40] - P-value for interaction between treatment group and Baseline third agent (bone-specific alkaline phosphatase)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [41]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.728
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.686
upper limit	0.773

Notes:

[41] - P value to assess difference between treatment groups (bone-specific alkaline phosphatase - NNRTI)

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [42]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.865
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.785
upper limit	0.954

Notes:

[42] - P value to assess difference between treatment groups (bone-specific alkaline phosphatase - INSTI)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [43]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.788
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.719
upper limit	0.864

Notes:

[43] - P value to assess difference between treatment groups (bone-specific alkaline phosphatase - PI)

Statistical analysis title	Statistical analysis 5
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other[44]
P-value	= 0.677 [45]
Method	ANCOVA

Notes:

[44] - Since statistical significance at the 10% level was not observed, results are presented overall only.

[45] - P-value for interaction between treatment group and Baseline third agent (procollagen type 1-N-propeptide)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [46]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.867

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.823
upper limit	0.914

Notes:

[46] - P value to assess difference between treatment groups (procollagen type 1-N-propeptide)

Statistical analysis title	Statistical analysis 7
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other[47]
P-value	< 0.001 [48]
Method	ANCOVA

Notes:

[47] - Since statistical significance at the 10% level was observed, results are presented separately per Baseline third agent.
[48] - P-value for interaction between treatment group and Baseline third agent (osteocalcin)

Statistical analysis title	Statistical analysis 8

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [49]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.853
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.799
upper limit	0.91

Notes:

[49] - P value to assess difference between treatment groups (osteocalcin - NNRTI)

Statistical analysis title	Statistical analysis 9

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.028 [50]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.886

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.796
upper limit	0.987

Notes:

[50] - P value to assess difference between treatment groups (osteocalcin - INSTI)

Statistical analysis title	Statistical analysis 10

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [51]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.743
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.672
upper limit	0.822

Notes:

[51] - P value to assess difference between treatment groups (osteocalcin - PI)

Statistical analysis title	Statistical analysis 11
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other[52]
P-value	= 0.782 [53]
Method	ANCOVA

Notes:

[52] - Since statistical significance at the 10% level was not observed, results are presented overall only.

[53] - P-value for interaction between treatment group and Baseline third agent (type 1 collagen cross-linked C-telopeptide)

Statistical analysis title	Statistical analysis 12

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for Baseline third agent class, age, sex, BMI category, smoking status and Baseline biomarker level.

Comparison groups	DTG + RPV v Current antiretroviral regimen

Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [54]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.818
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.751
upper limit	0.891

Notes:

[54] - P value to assess difference between treatment groups (type 1 collagen cross-linked C-telopeptide)

Secondary: Mean change from Baseline in interleukin 6 (IL-6) at Week 48

End point title	Mean change from Baseline in interleukin 6 (IL-6) at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess IL-6. Change from Baseline was calculated as value at indicated time point minus Baseline value.

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245[55]	237[56]		
Units: Nanograms (ng)/L				
arithmetic mean (standard deviation)				
Nanograms (ng)/L	-0.08 (± 2.373)	-0.07 (± 2.761)		

Notes:

[55] - Safety Population

[56] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from Baseline in insulin resistance based on homeostasis model assessment of insulin resistance (HOMA-IR) at Week 48

End point title	Mean change from Baseline in insulin resistance based on homeostasis model assessment of insulin resistance (HOMA-IR) at Week 48

End point description:

Blood biomarker samples were collected at Baseline (Day 1) and Week 48 to assess insulin resistance. Change from Baseline was calculated as value at indicated time point minus Baseline value. The homeostatic model assessment (HOMA) of insulin resistance (HOMA-IR) index , the product of basal glucose and insulin levels divided by 22.5, is regarded as a simple , inexpensive , and reliable surrogate

measure of insulin resistance .

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	237[57]	224[58]		
Units: HOMA-IR score				
arithmetic mean (standard deviation)				
Cateogry title 1	0.5 (± 4.78)	0.8 (± 3.938)		

Notes:

[57] - Safety Population

[58] - Safety Population

Statistical analyses

No statistical analyses for this end point

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

End point title	Mean 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 total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and triglycerides. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[59]	255[60]		
Units: Millimoles (mmol)/ L				
arithmetic mean (standard deviation)				
Total cholesterol, Week 24, n=237, 229	-0.015 (± 0.7539)	0.02 (± 0.5777)		
Total cholesterol, Week 48, n=237, 230	-0.079 (± 0.7926)	-0.038 (± 0.6148)		
LDL cholesterol calculation, Week 24, n=231, 221	0.085 (± 0.594)	0.055 (± 0.5232)		
LDL cholesterol calculation, Week 48, n=229, 220	-0.049 (± 0.6276)	-0.076 (± 0.528)		

HDL cholesterol direct, Week 24, n=237, 229	-0.024 (± 0.2365)	-0.051 (± 0.2258)		
HDL cholesterol direct, Week 48, n=237, 230	0.051 (± 0.2386)	0.049 (± 0.2489)		
Triglycerides, Week 24, n=237, 229	-0.184 (± 1.0102)	0.04 (± 0.9164)		
Triglycerides, Week 48, n=237, 230	-0.169 (± 1.0062)	-0.021 (± 1.0156)		

Notes:

[59] - Safety Population

[60] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Genotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria

End point title	Genotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria

End point description:

Genotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria are presented below. Confirmed Virologic Withdrawal (CVW) Population consisted of all participants in the ITT-E Population who met CVW (1 CVW per arm). 99999 indicates that data was not available. Genotypic Resistance Data only shown for Drugs Received for Participants Meeting Confirmed Virologic Withdrawal Criteria.

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[61]	0[62]		
Units: Participants				
INSTI, DTG, Susceptible	1			
INSTI, DTG, Potential low-level resistance	0			
INSTI, DTG, Low-level resistance	0			
INSTI, DTG, Intermediate resistance	0			
INSTI, DTG, High-level resistance	0			
NNRTI, RPV, Susceptible	0			
NNRTI, RPV, Potential low-level resistance	0			
NNRTI, RPV, Low-level resistance	0			
NNRTI, RPV, Intermediate resistance	1			
NNRTI, RPV, High-level resistance	0			

Notes:

[61] - CVW Population

[62] - CVW Population

Statistical analyses

No statistical analyses for this end point

Secondary: Phenotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria

End point title	Phenotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria

End point description:

Phenotypic resistance data for drugs received for participants meeting confirmed virologic withdrawal criteria are presented below. Confirmed Virologic Withdrawal (CVW) Population consisted of all participants in the ITT-E Population who met CVW (1 CVW per arm). 99999 indicate that data were not available based on drugs were not received. Phenotypic Resistance Data only shown for Drugs Received for Participants Meeting Confirmed Virologic Withdrawal Criteria.

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[63]	0[64]		
Units: Participants				
INI, DTG, Resistant	0			
INI, DTG, Partially Sensitive	0			
INI, DTG, Sensitive	1			
INI, RAL, Resistant	99999			
INI, RAL, Sensitive	99999			
INI, EVG, Resistant	99999			
INI, EVG, Sensitive	99999			
NNRTI, RPV, Resistant	0			
NNRTI, RPV, Sensitive	1			
NNRTI, ETR, Resistant	99999			
NNRTI, ETR, Partially Sensitive	99999			
NNRTI, ETR, Sensitive	99999			
NRTI, 3TC, Resistant	99999			
NRTI, 3TC, Sensitive	99999			
NRTI, ABC, Resistant	99999			
NRTI, ABC, Partially Sensitive	99999			
NRTI, ABC, Sensitive	99999			
NRTI, TDF, Resistant	99999			
NRTI, TDF, Partially Sensitive	99999			
NRTI, TDF, Sensitive	99999			
NRTI, d4T, Resistant	99999			
NRTI, d4T, Sensitive	99999			
NRTI, ddI, Resistant	99999			
NRTI, ddI, Partially Sensitive	99999			
NRTI, ddI, Sensitive	99999			
PI, ATV/r, Resistant	99999			
PI, ATV/r, Sensitive	99999			
PI, DRV/r, Resistant	99999			
PI, DRV/r, Partially Sensitive	99999			

PI, DRV/r, Sensitive	99999			
PI, FPV/r, Resistant	99999			
PI, FPV/r, Partially Sensitive	99999			
PI, FPV/r, Sensitive	99999			
PI, IDV/r, Resistant	99999			
PI, IDV/r, Sensitive	99999			
PI, LPV/r, Resistant	99999			
PI, LPV/r, Partially Sensitive	99999			
PI, LPV/r, Sensitive	99999			
PI, SQV/r, Resistant	99999			
PI, SQV/r, Partially Sensitive	99999			
PI, SQV/r, Sensitive	99999			
PI, TPV/r, Resistant	99999			
PI, TPV/r, Partially Sensitive	99999			
PI, TPV/r, Sensitive	99999			

Notes:

[63] - CVW Population

[64] - CVW Population. 99999 indicates not applicable based on drugs were not received.

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose concentrations of DTG and RPV at Weeks 4, 24 and 48 or withdrawal in participants switching to DTG + RPV

End point title	Pre-dose concentrations of DTG and RPV at Weeks 4, 24 and 48 or withdrawal in participants switching to DTG + RPV

End point description:

Two separate blood samples for DTG and RPV were collected pre-dose at Weeks 4, 24 and 48. Pre-dose concentrations of DTG and RPV at Weeks 4, 24 and 48 or withdrawal were summarized for the participants switching to DTG + RPV in the early switch phase. Pharmacokinetic (PK) Parameter Population consisted of all participants who received DTG +RPV and provided at least one evaluable estimate of predose concentration (C0). Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose at Week 4, 24 and 48 or at withdrawal visit

End point values	dtg 50 mg	rpv 25 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	242[65]	242[66]		
Units: ug/ L				
arithmetic mean (standard deviation)				
Week 4, n=176, 175	1578.88 (± 1170.967)	79.504 (± 38.2305)		
Week 24, n=207, 207	1447.23 (± 917.677)	90.207 (± 46.3022)		
Week 48, n=215, 215	1384.36 (± 889.829)	91.799 (± 47.1371)		

Notes:

[65] - PK Parameter Population

[66] - PK Parameter Population

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose concentrations of DTG and RPV at Weeks 2, 4 and 8 in the first 20 participants who switch from efavirenz (EFV) or nevirapine (NVP) to DTG + RPV

End point title	Pre-dose concentrations of DTG and RPV at Weeks 2, 4 and 8 in the first 20 participants who switch from efavirenz (EFV) or nevirapine (NVP) to DTG + RPV

End point description:

Two blood samples were collected pre-dose for DTG and RPV at Weeks 2 and 8 only for the first 20 participants who switch from EFV or NVP to DTG+RPV, in addition to the pre-dose blood sample collected at Week 4 for all subjects. One blood sample was collected pre-dose for EFV or NVP at Week 2 for the first 20 participants who switch from EFV or NVP to DTG + RPV. PK Parameter NNRTI Subset Extra Sampling Population consisted of the first approximately 20 participants in the PK Parameter NNRTI Subset population who have extra PK samples at weeks 2 and 8. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Pre-dose at Week 2, 4 and 8

End point values	dtg 50 mg	rpv 25 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	28[67]	28[68]		
Units: ug/ L				
arithmetic mean (standard deviation)				
Week 2, n=19, 19	834.58 (± 639.622)	57.342 (± 29.5436)		
Week 4, n=22, 21	1218.23 (± 842.703)	78.338 (± 31.4825)		
Week 8, n=26, 26	1472.5 (± 818.774)	79.652 (± 40.7546)		

Notes:

[67] - PK Parameter NNRTI Subset extra sampling Population

[68] - PK Parameter NNRTI Subset extra sampling Population

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV 1 RNA <50 c/mL at Week 48 using snapshot algorithm by Baseline third agent treatment class

End point title	Percentage of participants with plasma HIV 1 RNA <50 c/mL at Week 48 using snapshot algorithm by Baseline third agent treatment class

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL at Week 48 using the FDA snapshot algorithm was assessed by Baseline third agent class to assess the impact of Baseline third agent class (INSTI, NNRTI, or PI) on efficacy, safety and tolerability of DTG +RPV compared to continuation of CAR. Plasma samples were collected for HIV-1 RNA at Baseline (Day 1), Week 4, 8, 12, 24, 36 and 48. The analysis was done using cochran-mantel haenszel test stratified by current antiretroviral third-agent class. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[69]	255[70]		
Units: Percentage of participants				
NNRTI, n=144, 144	97	93		
INSTI, n=59, 49	92	94		
PI, n=58, 62	91	97		

Notes:

[69] - ITT-E Population

[70] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.179 [71]
Method	Chi-squared corrected

Notes:

[71] - One-sided p-value from weighted least squares chi-squared statistic. A p-value <=0.10 was used to indicate statistically significant evidence of heterogeneity in the difference in proportions across levels of each analysis strata.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

NNRTI: No formal non-inferiority margin has been pre-specified for secondary endpoints.

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	3.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	8.6

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
INSTI: No formal non-inferiority margin has been pre-specified for secondary endpoints.	
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-2.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.1
upper limit	7.4

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
PI: No formal non-inferiority margin has been pre-specified for secondary endpoints.	
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-5.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.9
upper limit	3.1

Secondary: Changes from Baseline in cluster designation (CD)4+ lymphocyte count at Week 48 by Baseline third agent treatment class

End point title	Changes from Baseline in cluster designation (CD)4+ lymphocyte count at Week 48 by Baseline third agent treatment class

End point description:

Blood for CD4 cell count assessment by flow cytometery was carried out at Baseline (Day 1), Week 4, 8, 12, 24, 36 and 48 to assess the impact of Baseline third agent class (INSTI, NNRTI, or PI) on efficacy, safety and tolerability of DTG +RPV compared to continuation of CAR. The full set of lymphocyte sub

sets was not evaluated. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Baseline and up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[72]	255[73]		
Units: Cells per mm^3				
arithmetic mean (standard deviation)				
NNRTI, n=139, 133	49.7 (± 166.4)	24.3 (± 160.32)		
INSTI, n=53, 46	-11.2 (± 176.56)	10.3 (± 155.53)		
PI, n=53, 61	10.5 (± 163.67)	12.2 (± 163.32)		

Notes:

[72] - ITT-E Population

[73] - ITT-E Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with any AE, AELD or AE with grade 1, 2, 3 or 4 toxicity over 48 weeks by Baseline third agent treatment class

End point title	Number of participants with any AE, AELD or AE with grade 1, 2, 3 or 4 toxicity over 48 weeks by Baseline third agent treatment class

End point description:

An AE is any untoward medical occurrence in a participant or clinical investigation participant, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Number of participants with any AE, AELD or AE with maximum grade toxicity experienced by any one participant over 48 weeks by Baseline third agent class (INSTI, NNRTI, or PI) was summarized. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[74]	255[75]		
Units: Participants				
Any AE, NNRTI, n=144, 144	106	96		

Any AE, INSTI, n=59, 49	47	36		
Any AE, PI, n=58, 62	42	42		
NNRTI, Maximum toxicity Grade 1 AE, n=144, 144	68	76		
NNRTI, Maximum toxicity Grade 2 AE, n=144, 144	30	19		
NNRTI, Maximum toxicity Grade 3 AE, n=144, 144	8	0		
NNRTI, Maximum toxicity Grade 4 AE, n=144, 144	0	1		
INSTI, Maximum toxicity Grade 1 AE, n=59, 49	27	20		
INSTI, Maximum toxicity Grade 2 AE, n=59, 49	15	15		
INSTI, Maximum toxicity Grade 3 AE, n=59, 49	5	1		
INSTI, Maximum toxicity Grade 4 AE, n=59, 49	0	0		
PI, Maximum toxicity Grade 1 AE, n=58, 62	24	26		
PI, Maximum toxicity Grade 2 AE, n=58, 62	14	13		
PI, Maximum toxicity Grade 3 AE, n=58, 62	3	3		
PI, Maximum toxicity Grade 4 AE, n=58, 62	1	0		
AELD, NNRTI, n=144, 144	5	1		
AELD, INSTI, n=59, 49	4	0		
AELD, PI, n=58, 62	3	0		

Notes:

[74] - Safety Population

[75] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-baseline emergent chemistry toxicities over 48 weeks by Baseline third agent treatment class

End point title	Number of participants with maximum post-baseline emergent chemistry toxicities over 48 weeks by Baseline third agent treatment class

End point description:

Blood samples were collected at Baseline (Day 1) and at Week 4, 8, 12, 24, 36 and 48 to evaluate ALT, albumin, ALP, AST, total bilirubin, chloride, creatinine, glucose, potassium, phosphate, sodium, BUN, total carbon dioxide, lipase, creatine phosphokinase and creatinine clearance. Change from Baseline was calculated as value at indicated time point minus Baseline value. Number of participants who experienced maximum toxicity grade post-baseline in chemistry parameters over 48 weeks by Baseline third agent treatment class (INSTI, NNRTI, PI) was summarized.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[76]	255[77]		
Units: Participants				
NNRTI, Grades 1, n=144, 144	51	52		
NNRTI, Grades 2, n=144, 144	31	40		
NNRTI, Grades 3, n=144, 144	7	4		
NNRTI, Grades 4, n=144, 144	1	5		
INSTI, Grades 1, n= 59, 49	19	11		
INSTI, Grades 2, n=59, 49	23	18		
INSTI, Grades 3, n= 59, 49	3	3		
INSTI, Grades 4, n= 59, 49	0	2		
PI, Grades 1, n= 58, 62	22	17		
PI, Grades 2, n= 58, 62	18	21		
PI, Grades 3, n= 58, 62	1	9		
PI, Grades 4, n= 58, 62	0	3		

Notes:

[76] - Safety Population

[77] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with maximum post-baseline emergent hematology toxicities over 48 weeks by Baseline third agent treatment class

End point title	Number of participants with maximum post-baseline emergent hematology toxicities over 48 weeks by Baseline third agent treatment class

End point description:

Blood samples were collected at Baseline (Day 1) and at Week 4, 8, 12, 24, 36 and 48 to evaluate hemoglobin, hematocrit, basophils, eosinophils, lymphocytes, monocytes, neutrophils, MCV, RBC count, WBC count and platelet count. Change from Baseline was calculated as value at indicated time point minus Baseline value. Number of participants who experienced maximum toxicity grade post-baseline in hematology parameters over 48 weeks by Baseline third agent treatment class (INSTI, NNRTI, PI) was summarized.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[78]	255[79]		
Units: Participants				
NNRTI; Grade 1; n= 144, 144	7	6		
NNRTI; Grade 2; n= 144, 144	1	2		
NNRTI; Grade 3; n= 144, 144	1	0		
NNRTI; Grade 4; n= 144, 144	1	0		

INI; Grade 1; n= 59, 49	1	1		
INI; Grade 2; n= 59, 49	0	0		
INI; Grade 3; n= 59, 49	0	0		
INI; Grade 4; n= 59, 49	0	0		
PI; Grade 1; n= 58, 62	3	4		
PI; Grade 2; n= 58, 62	1	0		
PI; Grade 3; n= 58, 62	2	0		
PI; Grade 4; n= 58, 62	0	0		

Notes:

[78] - Safety Population

[79] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with observed genotypic resistance for participants meeting virologic withdrawal criteria by Baseline third agent treatment class

End point title	Number of participants with observed genotypic resistance for participants meeting virologic withdrawal criteria by Baseline third agent treatment class

End point description:

For all participants who meet virologic withdrawal criteria, plasma samples with HIV-1 RNA level >=200 c/mL were to be analyzed in an attempt to obtain genotype data on as many samples as possible. Samples for drug resistance testing (genotypic) were to be collected at Day 1. Number of participants with genotypic resistance to CAR and to DTG or RPV for those meeting virologic withdrawal criteria in subgroups stratified based on Baseline third agent treatment class (INSTI, NNRTI, PI) were to be summarized. This outcome has not been analyzed as the number of participants was low (1 CVW per arm) and summaries by Baseline third agent were not provided. Therefore, data are not available for this outcome measure due to the insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[80]	0[81]		
Units: Participants				
Participants				

Notes:

[80] - CVW Population

[81] - CVW Population

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with observed phenotypic resistance for participants meeting virologic withdrawal criteria by Baseline third agent treatment class

End point title	Number of participants with observed phenotypic resistance for participants meeting virologic withdrawal criteria by Baseline third agent treatment class

End point description:

For all participants who meet virologic withdrawal criteria, plasma samples with HIV-1 RNA level >=200 c/mL were to be analyzed in an attempt to obtain phenotype data on as many samples as possible. Samples for drug resistance testing (phenotypic) were to be collected at Day 1. Number of participants with phenotypic resistance to CAR and to DTG or RPV for those meeting virologic withdrawal criteria in subgroups stratified based on Baseline third agent treatment class (INSTI, NNRTI, PI) were to be summarized. This outcome was not analyzed as the number of participants was low (1 CVW per arm) and summaries by Baseline third agent were not provided. Therefore, data are not available for this outcome measure due to the insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[82]	0[83]		
Units: Participants				
Participants				

Notes:

[82] - CVW Population

[83] - CVW Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in fasting lipids at Weeks 24 and 48 by Baseline third agent treatment class

End point title	Change from Baseline in fasting lipids at Weeks 24 and 48 by Baseline third agent treatment class

End point description:

Blood samples were collected at Baseline (Day 1), 24 and 48 to assess fasting lipids which included total cholesterol (CHO), LDL cholesterol, HDL cholesterol and triglycerides. Change from Baseline was calculated as value at indicated time point minus Baseline value. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles). 99999 indicates that data was not available.

End point type	Secondary

End point timeframe:

Baseline and up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[84]	255[85]		
Units: mmol/ L				
arithmetic mean (standard deviation)				
CHO, Week 24, overall, n=237, 229	1.015 (± 15.7472)	1.3 (± 12.2269)		
CHO, Week 48, overall, n=237, 230	-0.165 (± 15.9301)	0.194 (± 13.1071)		
CHO, Week 24, NNRTI, n=0, 132	99999 (± 99999)	1.238 (± 12.4889)		
CHO, Week 48, NNRTI, n=0, 128	99999 (± 99999)	0.281 (± 12.2469)		
CHO, Week 24, INSTI, n=0, 42	99999 (± 99999)	1.973 (± 12.1365)		
CHO, Week 48, INSTI, n=0, 44	99999 (± 99999)	2.798 (± 16.1468)		
CHO, Week 24, PI, n=0, 55	99999 (± 99999)	0.936 (± 11.853)		
CHO, Week 48, PI, n=0, 58	99999 (± 99999)	-1.971 (± 12.2195)		
HDL CHO direct, Overall, Week 24, n=237, 229	0.557 (± 19.4929)	-2.533 (± 16.3641)		
HDL CHO direct, Overall, Week 48, n=237,230	6.384 (± 20.9244)	4.723 (± 18.3253)		
HDL CHO direct, NNRTI, Week 24, n=0, 132	99999 (± 99999)	-2.562 (± 15.3521)		
HDL CHO direct, NNRTI, Week 48, n=0, 128	99999 (± 99999)	4.307 (± 17.8013)		
HDL CHO direct, INSTI, Week 24, n=0, 42	99999 (± 99999)	-3.097 (± 20.0002)		
HDL CHO direct, INSTI, Week 48, n=0, 44	99999 (± 99999)	5.386 (± 20.6791)		
HDL CHO direct, PI, Week 24, n=0, 55	99999 (± 99999)	-2.031 (± 15.9582)		
HDL CHO direct, PI, Week 48, n=0, 58	99999 (± 99999)	5.14 (± 17.8779)		
LDL CHO calculation, Overall, Week 24, n=231, 221	5.838 (± 22.9614)	4.395 (± 21.6685)		
LDL CHO calculation, Overall, Week 48, n=229, 220	1.137 (± 23.3849)	-0.598 (± 20.6931)		
LDL CHO calculation, NNRTI, Week 24, n=0, 129	99999 (± 99999)	5.959 (± 21.5692)		
LDL CHO calculation, NNRTI, Week 48, n=0, 124	99999 (± 99999)	0.747 (± 19.2299)		
LDL CHO calculation, INSTI, Week 24, n=0, 40	99999 (± 99999)	3.787 (± 17.6755)		
LDL CHO calculation, INSTI, Week 48, n=0, 42	99999 (± 99999)	2.647 (± 24.043)		
LDL CHO calculation, PI, Week 24, n=0, 52	99999 (± 99999)	0.983 (± 24.5052)		
LDL CHO calculation, PI, Week 48, n=0, 54	99999 (± 99999)	-6.212 (± 20.4774)		
Triglycerides, Overall, Week 24, n=237, 229	-0.825 (± 42.5565)	9.379 (± 45.5529)		
Triglycerides, Overall, Week 48, n=237, 230	1.169 (± 51.9844)	7.183 (± 44.7044)		
Triglycerides, NNRTI, Week 24, n=0, 132	99999 (± 99999)	4.962 (± 40.6201)		

Triglycerides, NNRTI, Week 48, n=0, 128	99999 (± 99999)	5.248 (± 41.7728)		
Triglycerides, INSTI, Week 24, n=0, 42	99999 (± 99999)	18.204 (± 47.2348)		
Triglycerides, INSTI, Week 48, n=0, 44	99999 (± 99999)	14.627 (± 56.2824)		
Triglycerides, PI, Week 24, n=0,55	99999 (± 99999)	13.241 (± 54.2327)		
Triglycerides, PI, Week 48, n=0, 58	99999 (± 99999)	5.806 (± 41.2106)		

Notes:

[84] - Safety Population

[85] - Safety Population

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in pre-specified treatment symptoms using the Symptom Distress Module at Weeks 4, 24 and 48 or withdrawal from the study

End point title	Change from Baseline in pre-specified treatment symptoms using the Symptom Distress Module at Weeks 4, 24 and 48 or withdrawal from the study

End point description:

The Symptom Distress Module, also called the HIV Symptom Index or Symptoms Impact Questionnaire, is a 20-item self-reported measure that addresses the presence and perceived distress linked to symptoms commonly associated with HIV or its treatment. Between and within treatment group comparisons were assessed on change from Baseline in pre-specified treatment symptoms using the Symptom Distress Module at Weeks 4, 24 and 48 or withdrawal from the study. Change from Baseline in Symptom count and symptom bother score have been summarized. The symptom bother score is based on the score for each symptom present ranging from 1 (it doesn't bother me) to 4 (it bothers me a lot). The symptom bother score ranges from 0 to 80. Last observation carried forward (LOCF) was used as primary method of analysis. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[86]	255[87]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Symptom count, Week 4, n=224, 229	-1.1 (± 4.11)	-0.8 (± 4.02)		
Symptom count, Week 24, n=228, 232	-0.7 (± 4.31)	-0.8 (± 4.64)		
Symptom count, Week 48, n=228, 231	-0.5 (± 4.33)	-0.4 (± 4.82)		
Symptom Bother Score, Week 4, n=224, 229	-2.8 (± 7.44)	-1.8 (± 7.24)		
Symptom Bother Score, Week 24, n=228, 232	-1.8 (± 8.4)	-1.7 (± 8.72)		
Symptom Bother Score, Week 48, n=228, 231	-1.5 (± 7.97)	-0.7 (± 9.3)		

Notes:
[86] - ITT-E Population
[87] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.43 [88]
Method	ANCOVA

Notes:
[88] - P-value for interaction between treatment group and Baseline symptom bother score (Week 4)

Statistical analysis title	Statistical analysis 2

Statistical analysis description:
Estimates are calculated from an ANCOVA model adjusting for age, Baseline third agent, gender, race and Baseline score.

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.039 [89]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.239
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.414
upper limit	-0.064

Notes:
[89] - P value to assess difference between treatment groups (Week 4)

Statistical analysis title	Statistical analysis 3
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.542 [90]
Method	ANCOVA

Notes:
[90] - P-value for interaction between treatment group and Baseline symptom bother score (Week 24)

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for age, Baseline third agent, gender, race and Baseline score.

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.448 [91]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.528
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.896
upper limit	0.84

Notes:

[91] - P value to assess difference between treatment groups (Week 24)

Statistical analysis title	Statistical analysis 5
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.402 [92]
Method	ANCOVA

Notes:

[92] - P-value for interaction between treatment group and Baseline symptom bother score (Week 48)

Statistical analysis title	Statistical analysis 6

Statistical analysis description:

Estimates are calculated from an ANCOVA model adjusting for age, Baseline third agent, gender, race and Baseline score.

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.164 [93]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.037
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.501
upper limit	0.426

Notes:

[93] - P value to assess difference between treatment groups (Week 48)

Secondary: Change from Baseline treatment satisfaction using the HIV treatment

satisfaction questionnaire (HIV TSQ) at Weeks 4, 24 and 48 or withdrawal from the study

End point title	Change from Baseline treatment satisfaction using the HIV treatment satisfaction questionnaire (HIV TSQ) at Weeks 4, 24 and 48 or withdrawal from the study

End point description:

The HIV TSQ is a 10-item self-reported scale that measures overall satisfaction with treatment and by specific domains e.g., convenience, flexibility. Each item is scored 0-6 where a higher score indicates the greater improvement in the past few weeks. These items are summed up to produce a treatment satisfaction total score (0 to 60) and 2 subscales: general satisfaction/clinical and lifestyle/ease subscales (0 to 30). The HIV TSQ was administered as a paper questionnaire. Between and within treatment group comparisons were assessed on change from Baseline treatment satisfaction using the HIV TSQ at Weeks 4, 24 and 48 or withdrawal from the study. Total score, lifestyle/ease score and General satisfaction/clinical sub-score (CS) have been summarized. LOCF was used as primary method of analysis. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles).

End point type	Secondary

End point timeframe:

Up to Week 48

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261[94]	255[95]		
Units: Score on a scale				
median (full range (min-max))				
Total score, Week 4, n=253, 250	0 (-21 to 23)	0 (-22 to 22)		
Total score, Week 24, n=257, 252	0 (-27 to 23)	0 (-24 to 24)		
Total score, Week 48, n=257, 251	0 (-27 to 25)	0 (-50 to 23)		
lifestyle/ease Sub-score, Week 4, n=252, 249	0 (-11 to 15)	0 (-11 to 7)		
lifestyle/ease Sub-score, Week 24, n=257, 251	0 (-18 to 14)	0 (-17 to 10)		
lifestyle/ease Sub-score, Week 48, n=257, 250	0 (-18 to 12)	0 (-21 to 11)		
General Satisfaction/CS, Week 4, n=253, 250	0 (-13 to 14)	0 (-17 to 15)		
General Satisfaction/CS, Week 24, n=257, 252	0 (-12 to 12)	0 (-15 to 15)		
General Satisfaction/CS, Week 48, n=257, 251	0 (-13 to 14)	0 (-29 to 14)		

Notes:

[94] - ITT-E Population

[95] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Current antiretroviral regimen v DTG + RPV

Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.037 [96]
Method	Wilcoxon rank sum test

Notes:

[96] - P-value to assess HIVTSQs Total Score difference between treatment groups (Week 4)

Statistical analysis title	Statistical analysis 2
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101 [97]
Method	Wilcoxon rank sum test

Notes:

[97] - P-value to assess HIVTSQs Total Score difference between treatment groups (Week 24)

Statistical analysis title	Statistical analysis 3
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.042 [98]
Method	Wilcoxon rank sum test

Notes:

[98] - P-value to assess HIVTSQs Total score difference between treatment groups (Week 48)

Statistical analysis title	Statistical analysis 4
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.132 [99]
Method	Wilcoxon rank sum test

Notes:

[99] - P-value to assess HIVTSQs lifestyle/ease sub- score difference between treatment groups (Week 4)

Statistical analysis title	Statistical analysis 5
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.022 [100]
Method	Wilcoxon rank sum test

Notes:

[100] - P-value to assess HIVTSQs lifestyle/ease sub- score difference between treatment groups (Week 24)

Statistical analysis title	Statistical analysis 6
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 [101]
Method	Wilcoxon rank sum test

Notes:

[101] - P-value to assess HIVTSQs lifestyle/ease sub- score difference between treatment groups (Week 48)

Statistical analysis title	Statistical analysis 7
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.076 [102]
Method	Wilcoxon rank sum test

Notes:

[102] - P-value to assess HIVTSQs General satisfaction/CS sub- score difference between treatment groups (Week 4)

Statistical analysis title	Statistical analysis 8
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073 [103]
Method	Wilcoxon rank sum test

Notes:

[103] - P-value to assess HIVTSQs General satisfaction/CS sub- score difference between treatment groups (Week 24)

Statistical analysis title	Statistical analysis 9
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	516
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.547 [104]
Method	Wilcoxon rank sum test

Notes:

[104] - P-value to assess HIVTSQs General satisfaction/CS sub- score difference between treatment groups (Week 48)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-treatment SAEs and non-serious AEs were collected from the start of the study treatment up to 52 weeks (until interim analysis). They are planned to be assessed up to 148 weeks and every 12 weeks after 148 weeks.

Adverse event reporting additional description:

On treatment SAEs and non-serious AEs were reported for the Safety Population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	DTG + RPV

Reporting group description:

Participants received DTG 50 milligrams (mg) + RPV 25 mg together once daily at approximately the same time, with a meal, in an open-label fashion up to Week 52 during early switch phase.

Reporting group title	Current antiretroviral regimen

Reporting group description:

Participants continued to receive their current antiretroviral regimen (two nucleoside reverse transcriptase inhibitor [NRTIs] + a third agent). A third agent included either of integrase strand transfer inhibitor integrase inhibitor (INSTI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or protease inhibitor (PI). CAR was administered according to the approved labeling in an open-label fashion up to Week 52 during early switch phase.

Serious adverse events	DTG + RPV	Current antiretroviral regimen	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 261 (6.90%)	9 / 255 (3.53%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Kaposi's sarcoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jarisch-Herxheimer reaction			

subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Eosinophilic pneumonia acute			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 261 (0.38%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			

subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Keratitis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 261 (0.00%)	1 / 255 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis chronic			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Haemarthrosis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 261 (0.77%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			

subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphogranuloma venereum			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periorbital cellulitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotavirus infection			
subjects affected / exposed	1 / 261 (0.38%)	0 / 255 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	DTG + RPV	Current antiretroviral regimen	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 261 (23.37%)	59 / 255 (23.14%)	
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 261 (6.51%)	6 / 255 (2.35%)	
occurrences (all)	36	6	

Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	17 / 261 (6.51%)	27 / 255 (10.59%)	
occurrences (all)	19	41	
Nasopharyngitis			
subjects affected / exposed	21 / 261 (8.05%)	22 / 255 (8.63%)	
occurrences (all)	26	24	
Bronchitis			
subjects affected / exposed	16 / 261 (6.13%)	10 / 255 (3.92%)	
occurrences (all)	19	12	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 February 2015	Protocol was amended to include additional pharmacokinetic visits for the first 20 participants in the NNRTI subset who switch from efavirenz (EFV) or nevirapine (NVP) in the early switch phase and additional pharmacokinetic visits for all participants in the late switch phase, addition of stratification by planned participation in the DEXA substudy, revisions to inclusion and exclusion criteria, revision to the definition of study completion, edits to the time and events table, revisions to suicidal risk monitoring section, and minor clarifications and corrections of typographical errors.
08 June 2015	Protocol was amended to include reasons for switch for PI-class aligned with other ART class switches, revisions to stratified analysis of the primary endpoint, revisions to virologic withdrawal Criteria, references to study drug versus investigational product, and minor clarifications and corrections of typographical errors.Protocol was amended to include reasons for switch for PI-class aligned with other ART class switches, revisions to stratified analysis of the primary endpoint, revisions to virologic withdrawal Criteria, references to study drug versus investigational product, and minor clarifications and corrections of typographical errors.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

DEXA sub-study 202094 (NCT02478632) Results available on ClinicalTrials.gov.

https://clinicaltrials.gov/ct2/show/results/NCT02478632?term=202094&rank=1

Notes: