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

Summary

EudraCT number	2014-005147-40
Trial protocol	ES DE NL BE GB IT
Global end of trial date	

Results information

Result version number	v2
This version publication date	14 October 2017
First version publication date	13 August 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	201636

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	14 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: 5
Country: Number of subjects enrolled	Australia: 10
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Canada: 29
Country: Number of subjects enrolled	France: 33
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Russian Federation: 35
Country: Number of subjects enrolled	Spain: 191
Country: Number of subjects enrolled	Taiwan: 54
Country: Number of subjects enrolled	United States: 86
Country: Number of subjects enrolled	United Kingdom: 3
Worldwide total number of subjects	510
EEA total number of subjects	291

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)	490
From 65 to 84 years	20
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 65 centers in 13 countries.

Pre-assignment

Screening details:

Total 669 participants were screened (159 failed), 510 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 switch 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	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.

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.

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 INI, 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	252	256
Completed	239	238
Not completed	13	18
Adverse event, serious fatal	-	1
Consent withdrawn by subject	3	7
Physician decision	-	2
Adverse event, non-fatal	6	1
Lost to follow-up	1	2
Lack of efficacy	2	1
Protocol deviation	1	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Total 699 participants were screened and 510 subjects 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	252	256	508
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	43.6	43.6	
standard deviation	± 10.93	± 10.76	-
Gender categorical Units: Subjects			
Female	58	51	109
Male	194	205	399
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	3	6	9
Japanese/East Asian (EA) Heritage (H.)/South EA H.	25	34	59
Black/African American	24	27	51
Native Hawaiian or other Pacific Islander	1	0	1
White	198	188	386
American Indian or Alaska Native and white	0	1	1
African American/African H. and Asian	1	0	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 Baseline (Day 1), Week 4, 8, 12, 24, 36 and 48. Treatment with DTG + RPV was 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	252[1]	256[2]		
Units: Percentage of participants				
Percentage of participants	95	96		

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, INI).

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Risk difference (RD)
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.3
upper limit	3

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	252[4]	256[5]		
Units: Cells per millimeter (mm)^3				
arithmetic mean (standard deviation)				
Week 24, n=247, 249	16.2 (± 150.34)	47.4 (± 179.68)		

Week 48, n=239, 245	32.3 (± 149.52)	41.8 (± 185.53)		

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	252[6]	256[7]		
Units: Percentage of participants				
Percentage of participants	98	96		

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, INI). 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	508
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	4

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, 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, 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, AELD or AE with maximum grade toxicity experienced over Week 48 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 52 weeks

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	252[8]	256[9]		
Units: Participants				
Common non-serious AE	65	68		
Any SAE	9	12		
Maximum Grade 1 AE	128	122		
Maximum toxicity Grade 2 AE	57	53		
Maximum toxicity Grade 3 AE	11	13		
Maximum toxicity Grade 4 AE	4	2		
AELD	9	2		

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

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	252[10]	256[11]		
Units: Participants				
Grade 1	95	78		
Grade 2	61	86		
Grade 3	22	23		
Grade 4	5	9		

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. 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.

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	252[12]	256[13]		
Units: Participants				
Grade 1	11	11		
Grade 2	3	2		
Grade 3	3	1		
Grade 4	0	1		

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 Week 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	234[14]	243[15]		
Units: mg/ Liter (L)				
arithmetic mean (standard deviation)				
mg/ Liter (L)	0.11 (± 5.379)	0.15 (± 4.944)		

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	237[16]	245[17]		
Units: mg/L				
arithmetic mean (standard deviation)				
mg/L	0 (± 0.113)	-0.01 (± 0.106)		

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	224[18]	238[19]		
Units: Nanomole (nmol)/L FEU				
arithmetic mean (standard deviation)	-0.02 (± 2.651)	0.02 (± 2.501)		

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	252[20]	256[21]		
Units: Nanogram/milliliter				
arithmetic mean (standard deviation)				
FABP, n=233, 242	-2.79 (± 3.007)	-1.93 (± 2.15)		
Soluble CD14, n=234, 242	379.72 (± 634.053)	754.54 (± 656.462)		

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	252[22]	256[23]		
Units: Microgram (ug)/Liter				
arithmetic mean (standard deviation)				
Soluble CD163, n=232, 241	50.18 (± 188.772)	54.26 (± 238.9)		

Oxidized LDL, n=234, 242	9.49 (± 745.962)	-41.3 (± 726.014)		

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	252[24]	256[25]		
Units: mg/ deciliter (dL)				
arithmetic mean (standard deviation)				
RBP, n=235, 243	-0.13 (± 1.023)	0.03 (± 0.974)		
Serum creatinine, n=238, 243	0.087 (± 0.1074)	0.011 (± 0.0876)		
Glucose, n=227, 227	0.762 (± 13.6194)	2.492 (± 12.1674)		

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	218[26]	224[27]		
Units: Millimoles (mmol)/ L				
arithmetic mean (standard deviation)				
Millimoles (mmol)/ L	-1.079 (± 16.9226)	-1.511 (± 15.8515)		

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. Urine biomarker samples were collected at Baseline (Day 1) and Week 48 to assess urine B2M and urine RBP. 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	252[28]	256[29]		
Units: Nanomoles (nmol)/ L				
arithmetic mean (standard deviation)				
B2M, blood, n=233, 241	-15.1452 (± 44.55903)	-4.5995 (± 38.90474)		
25 hydroxy-vitamin D, n=235, 244	-13.9 (± 22.76)	-8.2 (± 24.43)		
Urine B2M, n=89, 96	-128.2045 (± 726.38825)	39.8394 (± 253.43025)		
Urine RBP, n=221, 231	-8.8395 (± 28.83977)	-0.5851 (± 27.56405)		

Notes:

[28] - Safety Population

[29] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.275 [32]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.958
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.888
upper limit	1.034

Notes:

[32] - P value to assess difference between treatment groups (25 hydroxy-vitamin D - 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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.112 [33]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.902

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.793
upper limit	1.025

Notes:

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

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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [34]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.847
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.763
upper limit	0.942

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	252[35]	256[36]		
Units: Grams (g)/ mol				
arithmetic mean (standard deviation)				
Urine albumin/creatinine ratio, n=166, 171	-1.19 (± 3.916)	-2.59 (± 28.878)		

urine protein/creatinine ratio, n=176, 182	-5.63 (± 17.219)	-1.43 (± 42.832)		

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 I 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 I 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 I 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	252[37]	256[38]		
Units: ug/ L				
arithmetic mean (standard deviation)				
Bone-specific alkaline phosphatase, n=234, 244	-2.89 (± 4.024)	0.9 (± 4.129)		
Procollagen type 1 N-propeptide, n=234, 242	-9.1 (± 20.34)	-1.4 (± 18.95)		
Osteocalcin, n=233, 242	-4.4 (± 7.605)	-0.68 (± 6.579)		
Type I Collagen C-Telopeptides, n=234, 241	-0.18 (± 0.307)	-0.04 (± 1.16)		
sVCAM, n=234, 243	-2.21 (± 1291.994)	89.07 (± 1239.465)		

Notes:

[37] - Safety Population

[38] - Safety Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [41]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.724
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.679
upper limit	0.772

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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [42]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.825
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.742
upper limit	0.918

Notes:

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

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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [43]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.742
upper limit	0.884

Notes:

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

Statistical analysis title	Statistical analysis 5

Statistical analysis description:

Since statistical significance at the 10% level was not observed, results are presented overall only

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.677 [44]
Method	ANCOVA

Notes:

[44] - 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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [45]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.817

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.774
upper limit	0.863

Notes:

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

Statistical analysis title	Statistical analysis 7

Statistical analysis description:

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

Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001 [46]
Method	ANCOVA

Notes:

[46] - 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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [47]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.881
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.823
upper limit	0.943

Notes:

[47] - 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	Current antiretroviral regimen v DTG + RPV

Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.001 [48]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.829
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.93

Notes:

[48] - P value to assess difference between treatment groups (osteocalcin - INI)

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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [49]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.691
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.628
upper limit	0.759

Notes:

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

Statistical analysis title	Statistical analysis 11
Comparison groups	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other[50]
P-value	= 0.782 [51]
Method	ANCOVA

Notes:

[50] - Since statistical significance at the 10% level was not observed, results are presented overall only.
[51] - 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	Current antiretroviral regimen v DTG + RPV
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [52]
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.804
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.742
upper limit	0.872

Notes:

[52] - 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	233[53]	243[54]		
Units: Nanograms (ng)/ L				
arithmetic mean (standard deviation)				
Nanograms (ng)/ L	0.17 (± 2.736)	-0.18 (± 2.944)		

Notes:

[53] - Safety Population

[54] - 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 (1,2), 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	229[55]	237[56]		
Units: HOMA-IR Score				
arithmetic mean (standard deviation)				
HOMA-IR Score	-0.3 (± 5.74)	0.51 (± 3.53)		

Notes:

[55] - Safety Population

[56] - 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	252[57]	256[58]		
Units: mmol/ L				
arithmetic mean (standard deviation)				
Total cholesterol, Week 24, n=228, 223	0.076 (± 0.8398)	0.061 (± 0.7368)		
Total cholesterol, Week 48, n=221, 218	0.089 (± 0.8488)	0.064 (± 0.7197)		
LDL cholesterol calculation, Week 24, n=224, 217	0.165 (± 0.7065)	0.103 (± 0.6503)		
LDL cholesterol calculation, Week 48, n=215, 211	0.108 (± 0.7178)	0.029 (± 0.6134)		

HDL cholesterol direct, Week 24, n=228, 223	-0.03 (± 0.2601)	-0.044 (± 0.2394)		
HDL cholesterol direct, Week 48, n=221, 218	0.023 (± 0.2757)	0.018 (± 0.2722)		
Triglycerides, Week 24, n=228, 223	-0.154 (± 0.7324)	-0.001 (± 0.7712)		
Triglycerides, Week 48, n=221, 218	-0.093 (± 0.9767)	0.046 (± 0.8274)		

Notes:

[57] - Safety Population

[58] - 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 indicate that data was Not applicable based on drugs were not received. Genotypic Resistance Data only shown for Drugs Received for Participants Meeting Confirmed Virologic Withdrawal Criteria.

End point type	Secondary

End point timeframe:

Day 1

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[59]	1[60]		
Units: Participants				
NNRTI, RPV, Susceptible	1	99999		
NNRTI, RPV, Potential low-level resistance	0	99999		
NNRTI, RPV, Low-level resistance	0	99999		
NNRTI, RPV, Intermediate resistance	0	99999		
NNRTI, RPV, High-level resistance	0	99999		
INI, DTG, Susceptible	1	99999		
INI, DTG, Potential low-level resistance	0	99999		
INI, DTG, Low-level resistance	0	99999		
INI, DTG, Intermediate resistance	0	99999		
INI, DTG, High-level resistance	0	99999		
NRTI, FTC, Susceptible	99999	1		
NRTI, FTC, Potential low-level resistance	99999	0		
NRTI, FTC, Low-level resistance	99999	0		
NRTI, FTC, Intermediate resistance	99999	0		
NRTI, FTC, High-level resistance	99999	0		
NRTI, TDF, Susceptible	99999	1		

NRTI, TDF, Potential low-level resistance	99999	0		
NRTI, TDF, Low-level resistance	99999	0		
NRTI, TDF, Intermediate resistance	99999	0		
NRTI, TDF, High-level resistance	99999	0		
PI, DRV/r, Susceptible	99999	1		
PI, DRV/r, Potential low-level resistance	99999	0		
PI, DRV/r, Low-level resistance	99999	0		
PI, DRV/r, Intermediate resistance	99999	0		
PI, DRV/r, High-level resistance	99999	0		

Notes:

[59] - CVW Population

[60] - 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 was Not applicable 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:

Day 1

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1[61]	1[62]		
Units: Participants				
INI, DTG, Resistant	0	99999		
INI, DTG, Partially Sensitive	0	99999		
INI, DTG, Sensitive	1	99999		
INI, RAL, Resistant	99999	99999		
INI, RAL, Sensitive	99999	99999		
INI, EVG, Resistant	99999	99999		
INI, EVG, Sensitive	99999	99999		
NNRTI, RPV, Resistant	0	99999		
NNRTI, RPV, Sensitive	1	99999		
NNRTI, ETR, Resistant	99999	99999		
NNRTI, ETR, Partially Sensitive	99999	99999		
NNRTI, ETR, Sensitive	99999	99999		
NRTI, 3TC, Resistant	99999	99999		
NRTI, 3TC, Sensitive	99999	99999		

NRTI, ABC, Resistant	99999	99999		
NRTI, ABC, Partially Sensitive	99999	99999		
NRTI, ABC, Sensitive	99999	99999		
NRTI, FTC, Resistant	99999	0		
NRTI, FTC, Sensitive	99999	1		
NRTI, TDF, Resistant	99999	0		
NRTI, TDF, Partially Sensitive	99999	0		
NRTI, TDF, Sensitive	99999	1		
NRTI, d4T, Resistant	99999	99999		
NRTI, d4T, Sensitive	99999	99999		
NRTI, ddI, Resistant	99999	99999		
NRTI, ddI, Partially Sensitive	99999	99999		
NRTI, ddI, Sensitive	99999	99999		
PI, ATV/r, Resistant	99999	99999		
PI, ATV/r, Sensitive	99999	99999		
PI, DRV/r, Resistant	99999	0		
PI, DRV/r, Partially Sensitive	99999	0		
PI, DRV/r, Sensitive	99999	1		
PI, FPV/r, Resistant	99999	99999		
PI, FPV/r, Partially Sensitive	99999	99999		
PI, FPV/r, Sensitive	99999	99999		
PI, IDV/r, Resistant	99999	99999		
PI, IDV/r, Sensitive	99999	99999		
PI, LPV/r, Resistant	99999	99999		
PI, LPV/r, Partially Sensitive	99999	99999		
PI, LPV/r, Sensitive	99999	99999		
PI, SQV/r, Resistant	99999	99999		
PI, SQV/r, Partially Sensitive	99999	99999		
PI, SQV/r, Sensitive	99999	99999		
PI, TPV/r, Resistant	99999	99999		
PI, TPV/r, Partially Sensitive	99999	99999		
PI, TPV/r, Sensitive	99999	99999		

Notes:

[61] - CVW Population

[62] - CVW Population

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. Only those participants with data available at the specified time points were analyzed (represented by n=X, X in the category titles). Pharmacokinetic (PK) Parameter Population consisted of all participants who received DTG +RPV and provided at least one evaluable estimate of predose concentration (C0).

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	239[63]	239[64]		
Units: ug/ L				
arithmetic mean (standard deviation)				
Week 4, n=130, 130	1581.06 (± 1146.86)	92.046 (± 138.288)		
Week 24, n=210, 210	1835.68 (± 1120.539)	87.875 (± 39.1412)		
Week 48, n=215, 211	1915.11 (± 1304.238)	95.405 (± 48.2978)		

Notes:

[63] - PK Parameter Population

[64] - 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. 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	26[65]	26[66]		
Units: ug/ L				
arithmetic mean (standard deviation)				
Week 2, n=16, 15	821.25 (± 574.607)	65.36 (± 31.2965)		
Week 4, n=19, 19	994 (± 581.201)	67.374 (± 27.5663)		
Week 8, n=19, 19	1561.34 (± 1096.381)	77.416 (± 37.7129)		

Notes:

[65] - PK Parameter NNRTI Subset extra sampling Population

[66] - 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 (INI, NNRTI, or PI) on efficacy 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	252[67]	256[68]		
Units: Percentage of participants				
NNRTI, n=131, 134	95	98		
INI, n=46, 48	98	96		
PI, n=75, 74	95	92		

Notes:

[67] - ITT-E Population

[68] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.317 [69]
Method	Chi-squared corrected

Notes:

[69] - 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	508
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	-3.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.7
upper limit	1.5

Statistical analysis title	Statistical analysis 3
Statistical analysis description:	
INI: 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	508
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.1
upper limit	9

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	508
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Risk difference (RD)
Point estimate	2.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.3
upper limit	10.8

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 (INI, 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	252[70]	256[71]		
Units: Cells per mm^3				
arithmetic mean (standard deviation)				
NNRTI, n=124, 130	47.9 (± 142.9)	25 (± 151.27)		
INI, n=45, 46	19.9 (± 148.63)	39.9 (± 200.38)		
PI, n=70, 69	12.5 (± 160.27)	74.7 (± 227.78)		

Notes:

[70] - ITT-E Population

[71] - 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 (INI, 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	252[72]	256[73]		
Units: Participants				
Any AE, NNRTI, n=131, 134	102	98		
Any AE, INI, n=46, 48	38	34		
Any AE, PI, n=75, 74	60	58		
NNRTI, Maximum toxicity Grade 1 AE, n=131, 134	69	72		
NNRTI, Maximum toxicity Grade 2 AE, n=131, 134	27	23		
NNRTI, Maximum toxicity Grade 3 AE, n=131, 134	5	2		
NNRTI, Maximum toxicity Grade 4 AE, n=131, 134	1	1		
INI, Maximum toxicity Grade 1 AE, n=46, 48	28	20		
INI, Maximum toxicity Grade 2 AE, n=46, 48	7	12		
INI, Maximum toxicity Grade 3 AE, n=46, 48	2	2		
INI, Maximum toxicity Grade 4 AE, n=46, 48	1	0		
PI, Maximum toxicity Grade 1 AE, n=75, 74	31	30		
PI, Maximum toxicity Grade 2 AE, n=75, 74	23	18		
PI, Maximum toxicity Grade 3 AE, n=75, 74	4	9		
PI, Maximum toxicity Grade 4 AE, n=75, 74	2	1		
AELD, NNRTI, n=131, 134	3	0		
AELD, INI, n=46, 48	2	0		
AELD, PI, n=75, 74	4	2		

Notes:

[72] - Safety Population

[73] - 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 (INI, NNRTI, 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	252[74]	256[75]		
Units: Participants				
NNRTI, Grades 1, n=131, 134	47	42		
NNRTI, Grades 2, n=131, 134	32	48		
NNRTI, Grades 3, n=131, 134	13	13		
NNRTI, Grades 4, n=131, 134	2	3		
INI, Grades 1, n= 46, 48	13	11		
INI, Grades 2, n= 46, 48	19	15		
INI, Grades 3, n= 46, 48	1	1		
INI, Grades 4, n= 46, 48	3	2		
PI, Grades 1, n= 75, 74	35	25		
PI, Grades 2, n= 75, 74	10	23		
PI, Grades 3, n= 75, 74	8	9		
PI, Grades 4, n= 75, 74	0	4		

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 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	252[76]	256[77]		
Units: Participants				
NNRTI; Grade 1; n= 131, 134	5	3		
NNRTI; Grade 2; n= 131, 134	1	1		
NNRTI; Grade 3; n= 131, 134	1	1		
NNRTI; Grade 4; n= 131, 134	0	1		
INI; Grade 1; n= 46, 48	2	2		
INI; Grade 2; n= 46, 48	1	0		
INI; Grade 3; n= 46, 48	0	0		
INI; Grade 4; n= 46, 48	0	0		
PI; Grade 1; n= 75, 74	4	6		
PI; Grade 2; n= 75, 74	1	1		
PI; Grade 3; n= 75, 74	2	0		
PI; Grade 4; n= 75, 74	0	0		

Notes:

[76] - Safety Population

[77] - 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:

Day 1

End point values	DTG + RPV	Current antiretroviral regimen		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[78]	0[79]		
Units: Participants				
Participants				

Notes:

[78] - CVW Population

[79] - 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:

Day 1

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: 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 indicate that data were not available.

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	252[82]	256[83]		
Units: mmol/ mL				
arithmetic mean (standard deviation)				
CHO, Week 24, overall, n=228, 223	3.239 (± 18.1556)	2.375 (± 14.8357)		
CHO, Week 48, overall, n=221, 218	3.596 (± 18.7072)	2.472 (± 14.7202)		
CHO, Week 24, NNRTI, n=0, 118	99999 (± 99999)	3.383 (± 13.3685)		
CHO, Week 48, NNRTI, n=0, 118	99999 (± 99999)	4.099 (± 13.8992)		
CHO, Week 24, INI, n=0, 44	99999 (± 99999)	1.288 (± 14.8933)		
CHO, Week 48, INI, n=0, 43	99999 (± 99999)	0.524 (± 15.3143)		
CHO, Week 24, PI, n=0, 61	99999 (± 99999)	1.211 (± 17.3972)		
CHO, Week 48, PI, n=0, 57	99999 (± 99999)	0.575 (± 15.7475)		
HDL CHO direct, Overall, Week 24, n=228, 223	0.017 (± 18.7575)	-2.478 (± 16.6754)		
HDL CHO direct, Overall, Week 48, n=221, 218	3.975 (± 21.1039)	3.095 (± 18.8909)		
HDL CHO direct, NNRTI, Week 24, n=0, 118	99999 (± 99999)	0.062 (± 15.93)		
HDL CHO direct, NNRTI, Week 48, n=0, 118	99999 (± 99999)	4.818 (± 16.2253)		
HDL CHO direct, INI, Week 24, n=0, 44	99999 (± 99999)	-4.968 (± 16.2973)		
HDL CHO direct, INI, Week 48, n=0, 43	99999 (± 99999)	0.539 (± 22.6496)		
HDL CHO direct, PI, Week 24, n=0, 61	99999 (± 99999)	-5.594 (± 17.7923)		
HDL CHO direct, PI, Week 48, n=0, 57	99999 (± 99999)	1.457 (± 20.8346)		
LDL CHO calculation, Overall, Week 24, n=224, 217	11.504 (± 36.9087)	6.196 (± 24.0104)		
LDL CHO calculation, Overall, Week 48, n=215, 211	8.257 (± 33.0405)	3.258 (± 22.3644)		
LDL CHO calculation, NNRTI, Week 24, n=0, 116	99999 (± 99999)	6.816 (± 20.9081)		
LDL CHO calculation, NNRTI, Week 48, n=0, 114	99999 (± 99999)	4.92 (± 20.93)		

LDL CHO calculation, INI, Week 24, n=0, 44	99999 (± 99999)	6.355 (± 24.1747)		
LDL CHO calculation, INI, Week 48, n=0, 43	99999 (± 99999)	3.49 (± 23.3198)		
LDL CHO calculation, PI, Week 24, n=0, 57	99999 (± 99999)	4.813 (± 29.5705)		
LDL CHO calculation, PI, Week 48, n=0, 54	99999 (± 99999)	-0.434 (± 24.4332)		
Triglycerides, Overall, Week 24, n=228, 223	0.096 (± 55.6357)	8.649 (± 48.8249)		
Triglycerides, Overall, Week 48, n=221, 218	3.605 (± 54.4914)	11.068 (± 54.6321)		
Triglycerides, NNRTI, Week 24, n=0, 118	99999 (± 99999)	6.867 (± 44.8605)		
Triglycerides, NNRTI, Week 48, n=0, 118	99999 (± 99999)	10.215 (± 58.4055)		
Triglycerides, INI, Week 24, n=0, 44	99999 (± 99999)	8.386 (± 54.1265)		
Triglycerides, INI, Week 48, n=0, 43	99999 (± 99999)	4.644 (± 48.8708)		
Triglycerides, PI, Week 24, n=0, 61	99999 (± 99999)	12.283 (± 52.6943)		
Triglycerides, PI, Week 48, n=0, 57	99999 (± 99999)	17.681 (± 50.6912)		

Notes:

[82] - Safety Population

[83] - 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	252[84]	256[85]		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Symptom count, Week 4, n=212, 197	-1.6 (± 4.19)	0.2 (± 4.26)		
Symptom count, Week 24, n=214, 201	-0.8 (± 5.19)	-0.2 (± 4.06)		
Symptom count, Week 48, n=214, 201	-0.4 (± 5.52)	0 (± 4.49)		
Symptom Bother Score, Week 4, n=212, 197	-3 (± 7.25)	-0.8 (± 7.82)		
Symptom Bother Score, Week 24, n=214, 201	-1.7 (± 8.47)	-1.3 (± 8.53)		
Symptom Bother Score, Week 48, n=214, 201	-1.4 (± 8.32)	-0.7 (± 9.03)		

Notes:

[84] - ITT-E Population

[85] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.94 [86]
Method	ANCOVA

Notes:

[86] - 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	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [87]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-2.924
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.26
upper limit	-1.588

Notes:

[87] - P value to assess difference between treatment groups (Week 4)

Statistical analysis title	Statistical analysis 3

Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001 [88]
Method	ANCOVA

Notes:

[88] - 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	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.11 [89]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.192
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.656
upper limit	0.271

Notes:

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

Statistical analysis title	Statistical analysis 5
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.048 [90]
Method	ANCOVA

Notes:

[90] - 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	DTG + RPV v Current antiretroviral regimen

Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.038 [91]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-1.569
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.048
upper limit	-0.09

Notes:

[91] - 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	252[92]	256[93]		
Units: Scores on a scale				
median (full range (min-max))				
Total score, Week 4, n=250, 249	0 (-16 to 33)	0 (-25 to 21)		
Total score, Week 24, n=252, 254	1 (-18 to 33)	0 (-28 to 28)		
Total score, Week 48, n=252, 254	0.5 (-24 to 33)	0 (-28 to 20)		
lifestyle/ease Sub-score, Week 4, n=248, 249	0 (-7 to 15)	0 (-9 to 13)		
lifestyle/ease Sub-score, Week 24, n=252, 254	0 (-11 to 15)	0 (-14 to 12)		
lifestyle/ease Sub-score, Week 48, n=252, 254	0 (-13 to 16)	0 (-14 to 13)		

General Satisfaction/CS, Week 4, n=249, 249	0 (-10 to 18)	0 (-16 to 13)		
General Satisfaction/CS, Week 24, n=252, 254	0 (-7 to 18)	0 (-14 to 17)		
General Satisfaction/CS, Week 48, n=252, 254	0 (-14 to 18)	0 (-14 to 10)		

Notes:

[92] - ITT-E Population

[93] - ITT-E Population

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [94]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 2
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [95]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 3
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024 [96]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 4
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [97]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 5
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [98]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 6
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005 [99]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 7
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063 [100]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 8
Comparison groups	DTG + RPV v Current antiretroviral regimen
Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002 [101]
Method	Wilcoxon rank sum test

Notes:

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

Statistical analysis title	Statistical analysis 9
Comparison groups	DTG + RPV v Current antiretroviral regimen

Number of subjects included in analysis	508
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099 [102]
Method	Wilcoxon rank sum test

Notes:

[102] - 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 were 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	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 integrase inhibitor (INI), 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.

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.

Serious adverse events	Current antiretroviral regimen	DTG + RPV	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 256 (4.69%)	9 / 252 (3.57%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease mixed cellularity stage unspecified			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			

subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Plasmablastic lymphoma			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Wrist fracture			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Toxic encephalopathy			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (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			
Vertigo			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal fistula			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctitis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Panic attack			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (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			
Bronchitis			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			

subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 256 (0.00%)	1 / 252 (0.40%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroglossal cyst infection			
subjects affected / exposed	1 / 256 (0.39%)	0 / 252 (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	Current antiretroviral regimen	DTG + RPV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 256 (26.56%)	65 / 252 (25.79%)	
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 256 (6.64%)	23 / 252 (9.13%)	
occurrences (all)	19	24	

Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 16 / 256 (6.25%) 17	 21 / 252 (8.33%) 23	
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	 19 / 256 (7.42%) 19	 9 / 252 (3.57%) 10	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 28 / 256 (10.94%) 32	 28 / 252 (11.11%) 34	

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 EFV or 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.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported