Clinical trial results:
A Phase IIIb, Randomized, Multicenter, Active-controlled, Parallel-group, Non-inferiority, Open-label Study Evaluating the Efficacy, Safety, and Tolerability of Switching to Long-acting Cabotegravir Plus Long-acting Rilpivirine administered every two months from a Bictegravir/emtricitabine/tenofovir alafenamide Single Tablet Regimen in HIV-1 Infected Adults who are Virologically Suppressed

Summary

EudraCT number	2020-002623-11
Trial protocol	FR NL GB IE DE AT IT BE
Global end of trial date	17 April 2023

Results information

Result version number	v1
This version publication date	28 July 2023
First version publication date	28 July 2023

Trial information

Trial identification

Sponsor protocol code	213500

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04542070
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 GreatWest Road, Brentford,Middlesex, United Kingdom, TW8 9GS
Public contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, ViiV Healthcare, 1 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	17 August 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 July 2022
Global end of trial reached?	Yes
Global end of trial date	17 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferior antiviral activity of CAB LA + RPV LA every two months compared to a BIK single tablet regimen administered once daily over 12 months in suppressed HIV-1 infected antiretroviral therapy (ART)-experienced participants.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 November 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 22
Country: Number of subjects enrolled	Belgium: 15
Country: Number of subjects enrolled	Canada: 52
Country: Number of subjects enrolled	France: 33
Country: Number of subjects enrolled	Germany: 39
Country: Number of subjects enrolled	Ireland: 5
Country: Number of subjects enrolled	Japan: 20
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	Spain: 78
Country: Number of subjects enrolled	Switzerland: 16
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	United States: 286
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Italy: 86
Worldwide total number of subjects	687
EEA total number of subjects	274

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)	676
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Results presented are based on primary analysis (includes data up to Month12 [Maintenance Phase]). Data collection is ongoing and additional results will be provided after study completion. Any participants who successfully completed 12months of CAB+RPV treatment in Maintenance Phase could enter Extension Phase & continue to have access to CAB+RPV.

Pre-assignment

Screening details:

Total 687 were enrolled out of which 681 were included in intent-to-treat exposed population (ITT-E) that is all enrolled participants who received at least one dose of investigational product (IP) during the Maintenance Phase of the study (on or after Day 1). 6 participants did not receive any dose of IP.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Oral lead-in phase (OLI)

Arm description:

Participants with human immunodeficiency viruses (HIV)-1 who chose oral lead in (OLI) received oral 30 milligram (mg) Cabotegravir (CAB) tablet + 25 mg Rilpivirine (RPV) tablet once daily (QD) for one month. At the month 1 visit, the last dose of oral CAB + RPV was given, followed by the first 600 mg CAB long-acting (LA) + 900 mg RPV LA intramuscular injection (IM), and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections once every 2 months (Q2M) until Month 12.

Arm type	Experimental
Investigational medicinal product name	Cabotegravir (CAB) + Rilpivirine (RPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Injection
Routes of administration	Oral use, Intramuscular use

Dosage and administration details:

Participants with human immunodeficiency viruses (HIV)-1 who chose oral lead in (OLI) received oral 30 milligram (mg) Cabotegravir (CAB) tablet + 25 mg Rilpivirine (RPV) tablet once daily (QD) for one month. At the month 1 visit, the last dose of oral CAB + RPV was given, followed by the first 600 mg CAB long-acting (LA) + 900 mg RPV LA intramuscular injection (IM) and then once every 2 months (Q2M) until Month 12.

Arm title	Direct to injections (D2I)

Arm description:

Participants with HIV-1 who chose direct to injections (D2I) received the first injections of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading doses at Day 1 one month, followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and month 3 followed by Q2M until Month 11.

Arm type	Experimental
Investigational medicinal product name	CAB LA + RPV LA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants with HIV-1 who chose direct to injections (D2I) received the first injections of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading doses at Day 1 one month, followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and month 3 followed by Q2M until Month 11.

Arm title	Biktarvy (BIK)

Arm description:

Participants with HIV-1 received BIK tablet orally until month 12. BIK was a fixed dose combination of 50 mg Bictegravir (BIC) + 200 mg Emtricitabine (FTC) + 25 mg Tenofovir alafenamide (TAF).

Arm type	Active comparator
Investigational medicinal product name	Bictegravir (BIC) + Emtricitabine (FTC) + Tenofovir alafenamide (TAF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants with HIV-1 received BIK tablet orally until month 12. BIK was a fixed dose combination of 50 mg Bictegravir (BIC) + 200 mg Emtricitabine (FTC) + 25 mg Tenofovir alafenamide (TAF).

Number of subjects in period 1[1]	Oral lead-in phase (OLI)	Direct to injections (D2I)	Biktarvy (BIK)
Started	175	279	227
Completed	152	255	213
Not completed	23	24	14
Physician decision	1	-	1
Consent withdrawn by subject	5	8	9
Protocol Deviation	2	6	1
Adverse event, non-fatal	10	3	1
Protocol-Specified Withdrawal Criterion Met	1	1	-
Lost to follow-up	3	4	2
Lack of efficacy	1	2	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Worldwide 687 participants were enrolled, whereas 681 participants were actually included in the study.

Baseline characteristics

Reporting groups	
Reporting group title	Oral lead-in phase (OLI)
Reporting group description:	
Participants with human immunodeficiency viruses (HIV)-1 who chose oral lead in (OLI) received oral 30 milligram (mg) Cabotegravir (CAB) tablet + 25 mg Rilpivirine (RPV) tablet once daily (QD) for one month. At the month 1 visit, the last dose of oral CAB + RPV was given, followed by the first 600 mg CAB long-acting (LA) + 900 mg RPV LA intramuscular injection (IM), and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections once every 2 months (Q2M) until Month 12.	
Reporting group title	Direct to injections (D2I)
Reporting group description:	
Participants with HIV-1 who chose direct to injections (D2I) received the first injections of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading doses at Day 1 one month, followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and month 3 followed by Q2M until Month 11.	
Reporting group title	Biktarvy (BIK)
Reporting group description:	
Participants with HIV-1 received BIK tablet orally until month 12. BIK was a fixed dose combination of 50 mg Bictegravir (BIC) + 200 mg Emtricitabine (FTC) + 25 mg Tenofovir alafenamide (TAF).	

Reporting group values	Oral lead-in phase (OLI)	Direct to injections (D2I)	Biktarvy (BIK)
Number of subjects	175	279	227
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	38.5	39.0	38.6
standard deviation	± 11.38	± 11.09	± 11.41
Sex: Female, Male Units: Participants			
FEMALE	27	52	41
MALE	148	227	186
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	10	4	2
Asian - Central/South Asian Heritage	0	3	0
Asian - East Asian Heritage	1	0	2
Asian - Japanese Heritage	4	10	6
Asian - South East Asian Heritage	2	3	3
Black or African American	40	56	49
Native Hawaiian or Other Pacific Islander	0	0	1
White - Arabic/North African Heritage	10	5	10
White - White/Caucasian/European Heritage	104	194	149
Mixed White Race	0	0	1
Multiple	4	4	4

Reporting group values	Total		
Number of subjects	681		
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: Participants			
FEMALE	120		
MALE	561		
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	16		
Asian - Central/South Asian Heritage	3		
Asian - East Asian Heritage	3		
Asian - Japanese Heritage	20		
Asian - South East Asian Heritage	8		
Black or African American	145		
Native Hawaiian or Other Pacific Islander	1		
White - Arabic/North African Heritage	25		
White - White/Caucasian/European Heritage	447		
Mixed White Race	1		
Multiple	12		

End points

End points reporting groups

Reporting group title	Oral lead-in phase (OLI)

Reporting group description:

Participants with human immunodeficiency viruses (HIV)-1 who chose oral lead in (OLI) received oral 30 milligram (mg) Cabotegravir (CAB) tablet + 25 mg Rilpivirine (RPV) tablet once daily (QD) for one month. At the month 1 visit, the last dose of oral CAB + RPV was given, followed by the first 600 mg CAB long-acting (LA) + 900 mg RPV LA intramuscular injection (IM), and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections once every 2 months (Q2M) until Month 12.

Reporting group title	Direct to injections (D2I)

Reporting group description:

Participants with HIV-1 who chose direct to injections (D2I) received the first injections of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading doses at Day 1 one month, followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and month 3 followed by Q2M until Month 11.

Reporting group title	Biktarvy (BIK)

Reporting group description:

Participants with HIV-1 received BIK tablet orally until month 12. BIK was a fixed dose combination of 50 mg Bictegravir (BIC) + 200 mg Emtricitabine (FTC) + 25 mg Tenofovir alafenamide (TAF).

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

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Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
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Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Subject analysis set title	Q2M (OLI + D2I)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with HIV-1 who started OLI were administered with Cabotegravir and Rilpivirine (CAB + RPV) tablets orally for one month. At the month 1 visit, the last dose of oral 30 mg CAB + 25 mg RPV tablets were given, followed by the first 600 mg CAB LA + 900 mg RPV LA intramuscular injection, and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections every 2 months (Q2M) until Month 12. Participants with HIV-1 who started with D2I, received the first injection of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading dose at Day 1 followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and 3 followed by Q2M until Month 11.

Primary: Percentage of participants with plasma human immunodeficiency viruses (HIV)-1 ribonucleic acid (RNA) greater than or equal to (>=) 50 copies per milliliter (c/mL) at Month 12/11 - ITT-E Population

End point title	Percentage of participants with plasma human immunodeficiency viruses (HIV)-1 ribonucleic acid (RNA) greater than or equal to (>=) 50 copies per milliliter (c/mL) at Month 12/11 - ITT-E Population[1]

End point description:

Percentage of participants with plasma HIV 1 RNA >= 50 c/mL at month 12 was assessed using the food and drug administration (FDA) snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Primary

End point timeframe:

At month 12/11

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	454		
Units: Percentage of participants				
number (confidence interval 95%)	0.4 (0.0 to 2.4)	1.3 (0.5 to 2.9)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Biktarvy (BIK) v Q2M (OLI + D2I)
Number of subjects included in analysis	681
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	2.2

Statistical analysis title	Statistical Analysis 2
Comparison groups	Biktarvy (BIK) v Q2M (OLI + D2I)
Number of subjects included in analysis	681
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted difference in percentage
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.5
upper limit	2.2

Primary: Percentage of participants with plasma HIV-1 RNA greater >=50 copies per milliliter (c/mL) at Month 12/11 - mITT-E Population

End point title	Percentage of participants with plasma HIV-1 RNA greater >=50 copies per milliliter (c/mL) at Month 12/11 - mITT-E Population[2]

End point description:

Percentage of participants with plasma HIV 1 RNA >= 50 c/mL at month12 was assessed using the food and drug administration (FDA) snapshot algorithm. For Q2M arm, data from Q2MOLI at Month12 visit and Q2M D2I at Month 11 visit were combined as study objective was to demonstrate the non-inferior antiviral activity of (Q2M)(OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month12 visit. The FDA snapshot algorithm defines participant's virologic response status using only

viral load at predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. Third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately. Modified intent-to-treat exposed (mITT-E) population included all ITT-E participants excluding those from GSK Investigational site where Good Clinical Practice noncompliance was observed

End point type	Primary

End point timeframe:

At month 12/11

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: Percentage of participants				
number (confidence interval 95%)	0.4 (0.0 to 2.5)	1.1 (0.4 to 2.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Biktarvy (BIK) v Q2M (OLI + D2I)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.6
upper limit	2

Statistical analysis title	Statistical Analysis 2
Comparison groups	Biktarvy (BIK) v Q2M (OLI + D2I)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Adjusted difference in percentage
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	2

Secondary: Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 12/11 -mITT-E Population

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 12/11 -mITT-E Population[3]

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL was assessed using the FDA snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Secondary

End point timeframe:

At month 12/11

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: Percentage of participants				
number (confidence interval 95%)	92.8 (89.4 to 96.2)	90.2 (87.4 to 92.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV-1 RNA less than (<)50 c/mL at Month 12/11 - ITT-E Population

End point title	Percentage of participants with plasma HIV-1 RNA less than (<)50 c/mL at Month 12/11 - ITT-E Population[4]

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL was assessed using the FDA snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Secondary

End point timeframe:

At month 12/11

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	454		
Units: Percentage of participants				
number (confidence interval 95%)	93.0 (89.6 to 96.3)	89.4 (86.6 to 92.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 6/5 - ITT-E Population

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 6/5 - ITT-E Population[5]

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL was assessed using the FDA snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Secondary

End point timeframe:

At month 6/5

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	454		
Units: Percentage of participants				
number (confidence interval 95%)	97.8 (95.9 to 99.7)	92.7 (90.3 to 95.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 6/5 - mITT-E Population

End point title	Percentage of participants with plasma HIV-1 RNA <50 c/mL at Month 6/5 - mITT-E Population[6]

End point description:

Percentage of participants with plasma HIV 1 RNA < 50 c/mL was assessed using the FDA snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Secondary

End point timeframe:

At month 6/5

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: Percentage of participants				
number (confidence interval 95%)	97.8 (95.8 to 99.7)	93.5 (91.2 to 95.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of HIV viral load - mITT-E population

End point title	Absolute values of HIV viral load - mITT-E population[7]

End point description:

Plasma samples were collected for quantitative analysis of HIV-1 RNA. Logarithm to base 10 (log10) values for plasma HIV-1 RNA has been presented. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: log10 concentration per milliliter(c/mL)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	1.5947 (± 0.06640)	1.5993 (± 0.10559)		
Month 6/5	1.5910 (± 0.01182)	1.6002 (± 0.09268)		
Month 12/11	1.5911 (± 0.01552)	1.6019 (± 0.13064)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with protocol-defined confirmed virologic failure (CVF) through Month 6/5 and 12/11 - mITT-E population

End point title	Number of participants with protocol-defined confirmed virologic failure (CVF) through Month 6/5 and 12/11 - mITT-E population[8]

End point description:

Protocol-defined confirmed virologic failure was defined as rebound as indicated by two consecutive plasma HIV-1 RNA levels >= 200 c/mL (Day 1 values are not applicable) after prior suppression to <200 c/mL. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at Month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. Cumulative number of participants with protocol defined CVF through Month 6/5 and 12/11 has been presented.

End point type	Secondary

End point timeframe:

Up to month 12

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: Participants				
Month 6/5	0	1		
Month 12/11	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with plasma HIV-1 RNA greater than or equal to (>=) 50 c/mL at Month 6/5 - mITT-E population

End point title	Percentage of participants with plasma HIV-1 RNA greater than or equal to (>=) 50 c/mL at Month 6/5 - mITT-E population[9]

End point description:

Percentage of participants with plasma HIV 1 RNA >= 50 c/mL at month 6 was assessed using the food and drug administration (FDA) snapshot algorithm. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. The FDA snapshot algorithm defines a participant's virologic response status using only the viral load at the predefined time point within a window of time (HIV-RNA equal to or above 50 copies/mL and HIV-RNA below 50 copies/mL), along with study drug discontinuation status. The third category of the FDA snapshot ("No virologic data") is not pre-defined as an endpoint and therefore not reported separately.

End point type	Secondary

End point timeframe:

At month 6/5

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: Percentage of participants				
number (confidence interval 95%)	0 (0.0 to 1.6)	0.4 (0.1 to 1.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in HIV viral load - mITT-E population

End point title	Change from baseline in HIV viral load - mITT-E population[10]

End point description:

Plasma samples were collected for quantitative analysis of HIV-1 RNA. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. Logarithm to base 10 values for plasma HIV-1 RNA has been presented. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: log10 c/mL				
arithmetic mean (standard deviation)				
Baseline (Day 1)	1.5947 (± 0.06640)	1.5993 (± 0.10559)		
Month 6/5	-0.0039 (± 0.06826)	0.0015 (± 0.13997)		
Month 12/11	-0.0041 (± 0.07172)	0.0029 (± 0.17038)		

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of cluster of differentiation 4 plus (CD4+) cell count - mITT-E population

End point title	Absolute values of cluster of differentiation 4 plus (CD4+) cell count - mITT-E population[11]

End point description:

Blood samples were collected and CD4+ cell count was assessed using flow cytometry. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	222	447		
Units: cells per cubic millimeter(cells/mm^3)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	679.4 (± 306.89)	670.9 (± 282.11)		
Month 6/5	673.7 (± 290.46)	689.1 (± 284.89)		
Month 12/11	717.3 (± 317.82)	711.9 (± 297.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ cell count - mITT-E population

End point title	Change from Baseline in CD4+ cell count - mITT-E

End point description:

Blood samples were collected and CD4+ cell count was assessed using flow cytometry. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	447		
Units: cells/mm^3				
arithmetic mean (standard deviation)				
Baseline (Day 1)	679.4 (± 306.89)	670.9 (± 282.11)		
Month 6/5	-3.1 (± 197.62)	20.4 (± 202.38)		
Month 12/11	32.2 (± 208.29)	35.2 (± 219.79)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent phenotypic resistance through Month 12/11 - Confirmed Virologic Failure (CVF) population

End point title	Number of participants with treatment-emergent phenotypic resistance through Month 12/11 - Confirmed Virologic Failure (CVF) population

End point description:

Blood samples were collected to evaluate the phenotypic resistance to CAB, RPV, BIC, FTC, and TAF. For each participant, prevalence of phenotype, fold changes to CAB, RPV, and BIC, replication capacity of Integrase, protease, and reverse transcriptase enzymes at the time of CVF was assessed. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. Confirmed Virologic Failure (CVF) population included all participants in the ITT-E population who met Confirmed Virologic Failure (CVF). No participants in the BIK arm met CVF.

End point type	Secondary

End point timeframe:

Up to Month 12/11

End point values	Q2M (OLI + D2I)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Participants				
NNRTI	2			
IN	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent genotypic resistance through Month 12/11 - CVF population

End point title	Number of participants with treatment-emergent genotypic resistance through Month 12/11 - CVF population

End point description:

Blood samples were collected to evaluate the genotypic resistance to CAB, RPV, BIC, FTC, and TAF. For each participant, prevalence of resistance mutations and genotypic susceptibility at the time of CVF was assessed. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. No participants in the BIK arm met CVF.

End point type	Secondary

End point timeframe:

Up to Month 12/11

End point values	Q2M (OLI + D2I)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: Participants				
M230L	1			
Q148R	1			
K101E	1			
G118R	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent genotypic resistance through Month 6/5 - CVF population

End point title	Number of participants with treatment-emergent genotypic resistance through Month 6/5 - CVF population

End point description:

Blood samples were collected to evaluate the genotypic resistance to CAB, RPV, BIC, FTC, and TAF. For each participant, prevalence of resistance mutations and genotypic susceptibility at the time of CVF was assessed. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. No participants in the BIK arm met CVF.

End point type	Secondary

End point timeframe:

Up to Month 6/5

End point values	Q2M (OLI + D2I)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: Participants				
M230L	1			
Q148R	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with treatment-emergent phenotypic resistance through Month 6/5 - CVF population

End point title	Number of participants with treatment-emergent phenotypic resistance through Month 6/5 - CVF population

End point description:

Blood samples were collected to evaluate the phenotypic resistance to CAB, RPV, BIC, FTC, and TAF. For each participant, prevalence of phenotype, fold changes to CAB, RPV, and BIC, replication capacity of Integrase, protease, and reverse transcriptase enzymes at the time of CVF was assessed. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. No participants in the BIK arm met CVF.

End point type	Secondary

End point timeframe:

Up to Month 6/5

End point values	Q2M (OLI + D2I)			
Subject group type	Subject analysis set			
Number of subjects analysed	1			
Units: Participants				
NNRTI	1			
IN	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in bone biomarkers: specific alkaline phosphatase, procollagen type 1 N-Terminal propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin (micrograms per liter (ug/L)) - Safety population

End point title	Change from baseline in bone biomarkers: specific alkaline phosphatase, procollagen type 1 N-Terminal propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin (micrograms per liter (ug/L)) - Safety population[13]

End point description:

Serum samples were collected to evaluate bone specific biomarkers: specific alkaline phosphatase, procollagen type 1 N-propeptide, type 1 collagen cross-linked C-telopeptide, osteocalcin. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For Q2M arm, data from Q2M OLI participants at Month6 and 12 visit and Q2MD2I participants at Month5 and 11 visit were combined as study objective was to demonstrate non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. Safety Population included all randomly assigned participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	449		
Units: micrograms per liter (ug/L)				
arithmetic mean (standard deviation)				
BoneSpecificAlkalinePhosphatase,Baseline(Day 1)	12.9 (± 4.60)	12.7 (± 4.27)		
BoneSpecificAlkalinePhosphatase,Month6/5	0.2 (± 2.60)	0.3 (± 9.89)		
BoneSpecificAlkalinePhosphatase,Month12/11	0.5 (± 3.55)	0.1 (± 5.03)		
Osteocalcin,Baseline(Day 1)	20.4 (± 7.48)	21.0 (± 7.35)		
Osteocalcin,Month6/5	-0.4 (± 5.11)	0.4 (± 5.53)		
Osteocalcin,Month12/11	-0.6 (± 5.51)	0.9 (± 6.11)		
Procollagen1N-TerminalPropeptide,Baseline(Day 1)	59.2 (± 23.88)	59.1 (± 23.06)		
Procollagen1N-Terminal Propeptide,Month6/5	0.1 (± 18.53)	-1.5 (± 15.70)		
Procollagen1N-Terminal Propeptide,Month12/11	0.6 (± 19.63)	-0.7 (± 19.73)		
TypeICollagenC-Telopeptides,Baseline(Day 1)	0.5 (± 0.25)	0.4 (± 0.25)		
TypeICollagen C-Telopeptides,Month6/5	-0.1 (± 0.21)	-0.1 (± 0.23)		
TypeICollagen C-Telopeptides,Month12/11	0.0 (± 0.22)	0.0 (± 0.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal biomarkers: specific serum beta-2 microglobulin, cystatin c, retinol binding protein, urine beta-2 microglobulin (milligrams per liter [mg/L]) - Safety population

End point title	Change from baseline in renal biomarkers: specific serum beta-2 microglobulin, cystatin c, retinol binding protein, urine beta-2 microglobulin (milligrams per liter [mg/L]) - Safety population[14]

End point description:

Serum samples were collected to evaluate renal specific biomarkers: specific serum beta-2 microglobulin, cystatin c, retinol binding protein, urine beta-2 microglobulin. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	448		
Units: milligrams per liter (mg/L)				
arithmetic mean (standard deviation)				
Serum beta-2 microglobulin, Baseline (Day 1)	1.8 (± 0.38)	1.8 (± 0.40)		
Serum beta-2 microglobulin, Month 6/5	0.0 (± 0.28)	0.0 (± 0.28)		
Serum beta-2 microglobulin, Month 12/11	0.0 (± 0.32)	0.0 (± 0.33)		
Serum cystatin C, Baseline (Day 1)	0.9 (± 0.14)	0.9 (± 0.13)		
Serum cystatin C, Month 6/5	0.0 (± 0.08)	0.0 (± 0.08)		
Serum cystatin C, Month 12/11	0.0 (± 0.08)	0.0 (± 0.08)		
Serum retinol binding protein, Baseline (Day 1)	52.2 (± 12.61)	51.3 (± 13.01)		
Serum retinol binding protein, Month 6/5	-0.3 (± 8.75)	-1.0 (± 9.00)		
Serum retinol binding protein, Month 12/11	0.2 (± 9.06)	-1.2 (± 9.24)		
Urine beta-2 microglobulin, Baseline (Day 1)	0.2 (± 0.40)	0.2 (± 0.34)		
Urine beta-2 microglobulin, Month 6/5	0.1 (± 0.65)	0.0 (± 0.40)		
Urine beta-2 microglobulin, Month 12/11	0.1 (± 0.52)	0.0 (± 0.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in bone biomarkers: serum 25-hydroxyvitamin D (nanomoles per liter (nmol/L)) - Safety population

End point title	Change from baseline in bone biomarkers: serum 25-hydroxyvitamin D (nanomoles per liter (nmol/L)) - Safety population[15]

End point description:

Serum samples were collected to evaluate bone specific biomarkers: serum 25-hydroxyvitamin D. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	219	440		
Units: nanomoles per liter (nmol/L)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	59.9 (± 33.30)	61.0 (± 34.69)		
Month 6/5	6.0 (± 34.16)	2.8 (± 29.24)		
Month 12/11	-3.1 (± 26.38)	-2.3 (± 29.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal biomarker: urine retinol binding protein 4 (microgram per liter (ug/L)) - Safety population

End point title	Change from baseline in renal biomarker: urine retinol binding protein 4 (microgram per liter (ug/L)) - Safety population[16]

End point description:

Serum samples were collected to evaluate renal specific biomarkers: urine retinol binding protein 4. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	222	447		
Units: microgram per liter (ug/L)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	100.0 (± 82.00)	114.2 (± 111.45)		
Month 6/5	5.7 (± 105.08)	0.8 (± 139.88)		
Month 12/11	-1.2 (± 105.26)	-0.6 (± 123.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal biomarkers: urine phosphate (millimoles per liter (mmol/L)) - Safety population

End point title	Change from baseline in renal biomarkers: urine phosphate (millimoles per liter (mmol/L)) - Safety population[17]

End point description:

Serum samples were collected to evaluate renal specific biomarkers: urine phosphate. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	223	449		
Units: millimoles per liter (mmol/L)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	18.4 (± 13.10)	20.0 (± 14.03)		
Month 6/5	0.4 (± 15.60)	-1.0 (± 16.29)		
Month 12/11	-0.6 (± 15.16)	0.1 (± 16.17)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal biomarker: urine retinol binding protein/creatinine (milligram per mole (mg/mol)) - Safety population

End point title	Change from baseline in renal biomarker: urine retinol binding protein/creatinine (milligram per mole (mg/mol)) - Safety population[18]

End point description:

Serum samples were collected to evaluate renal specific biomarkers: urine retinol binding protein/creatinine. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	107	216		
Units: milligram per mole (mg/mol)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	8.0 (± 5.75)	8.6 (± 6.32)		
Month 6/5	-0.8 (± 7.23)	0.8 (± 6.00)		
Month 12/11	0.0 (± 4.15)	-0.5 (± 6.41)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in renal biomarker: urine beta-2 microglobulin/ creatinine (grams per mole (g/mol)) - Safety population

End point title	Change from baseline in renal biomarker: urine beta-2 microglobulin/ creatinine (grams per mole (g/mol)) - Safety population[19]

End point description:

Serum samples were collected to evaluate renal specific biomarkers: urine beta-2 microglobulin/ creatinine. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	88	182		
Units: grams per mole (g/mol)				
arithmetic mean (standard deviation)				
Baseline (Day 1)	0.0 (± 0.04)	0.0 (± 0.03)		
Month 6/5	0.0 (± 0.19)	0.0 (± 0.03)		

Month 12/11	0.0 (± 0.04)	0.0 (± 0.02)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in percentage of participants with metabolic syndrome at month 12/11 - Safety population

End point title	Change From Baseline in percentage of participants with metabolic syndrome at month 12/11 - Safety population[20]

End point description:

Metabolic syndrome defined as cluster of conditions that occurred together increasing one's risk of heart disease, stroke and type 2 diabetes mellitus (DM). These conditions included increased blood pressure (BP), elevated blood glucose levels, excess body fat around the waist and abnormal fasting cholesterol and triglyceride (TG) levels. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Month 12/11

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	454		
Units: Percentage of participants				
Yes (Baseline) to Yes (Month 12/11)	9	9		
Yes (Baseline) to No (Month 12/11)	7	5		
Yes (Baseline) to Missing (Month 12/11)	1	2		
No (Baseline) to Yes (Month 12/11)	8	6		
No (Baseline) to No (Month 12/11)	70	69		
No (Baseline) to Missing ((Month 12/11))	6	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in homeostasis model of assessment-insulin

resistance (HOMA-IR) - Safety population

End point title	Change from baseline in homeostasis model of assessment-insulin resistance (HOMA-IR) - Safety population[21]

End point description:

The homeostatic model assessment (HOMA) is a method used to quantify insulin resistance. HOMA-IR is calculated as fasting insulin microunits per liter (microU/L) multiplied by fasting glucose (nmol/L) divided by 22.5. Higher HOMA-IR values indicate increased insulin resistance; values <2 is generally regarded as normal. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	210	409		
Units: HOMA-IR score				
arithmetic mean (standard deviation)				
Baseline (Day 1)	3.1 (± 5.06)	2.8 (± 4.05)		
Month 6/5	-0.1 (± 5.09)	0.3 (± 4.11)		
Month 12/11	-0.4 (± 3.76)	0.2 (± 3.99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in percentage of participants with metabolic syndrome at month 6/5 - Safety population

End point title	Change From Baseline in percentage of participants with metabolic syndrome at month 6/5 - Safety population[22]

End point description:

Metabolic syndrome defined as cluster of conditions that occurred together increasing one's risk of heart disease, stroke and type 2 diabetes mellitus (DM). These conditions included increased blood pressure (BP), elevated blood glucose levels, excess body fat around the waist and abnormal fasting cholesterol and triglyceride (TG) levels. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 visit and Q2M D2I participants at Month 5 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at month 6/5

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	227	454		
Units: Percentage of participants				
Yes (Baseline) to Yes (Month 6/5)	11	9		
Yes (Baseline) to No (Month 6/5)	6	7		
Yes (Baseline) to Missing (Month 6/5)	0	1		
No (Baseline) to Yes (Month 6/5)	10	5		
No (Baseline) to No (Month 6/5)	71	74		
No (Baseline) to Missing (Month 6/5)	2	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment preference as assessed using preference questionnaire at month 12/11 - Q2M - mITT-E population

End point title	Percentage of participants with treatment preference as assessed using preference questionnaire at month 12/11 - Q2M - mITT-E population[23]

End point description:

Participants who had switched from the daily oral BIK regimen to CAB + RPV, were assessed as per the preference questionnaire every two months. There were 3 preference questions included to assess the preferred treatment 1) Long-acting injectable HIV medication, 2) Daily oral HIV medication, 3) No Preference. This endpoint was only planned to be analyzed for Q2M arm only. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit. Data represented included maintenance withdrawal or Month 12/11.

End point type	Secondary

End point timeframe:

Up to month 12/11

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Oral lead-in phase (OLI)	Direct to injections (D2I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	262		
Units: Percentage of participants				
Long-acting injectable HIV medication	87	92		
Daily oral HIV medication	7	4		
No Preference	6	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in individual item scores using HIVTSQs - mITT-E population

End point title	Change from baseline in individual item scores using HIVTSQs - mITT-E population[24]

End point description:

The individual item scores on HIVTSQs scale were rated on a scale of 6 (very satisfied, convenient, flexible, etc.) to -6 (very dissatisfied, inconvenient, inflexible, etc.). Higher scores represent greater satisfaction with each aspect of treatment. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	222	446		
Units: Scores on scale				
arithmetic mean (standard deviation)				
Item 1, Baseline (Day 1)	5.6 (± 0.75)	5.5 (± 0.86)		
Item 1, Month 6/5	-0.2 (± 0.91)	0.1 (± 1.10)		
Item 1, Month 12/11	-0.3 (± 1.00)	0.2 (± 1.07)		
Item 2, Baseline (Day 1)	5.8 (± 0.45)	5.8 (± 0.54)		
Item 2, Month 6/5	-0.1 (± 0.55)	0.0 (± 0.80)		
Item 2, Month 12/11	-0.1 (± 0.69)	0.0 (± 0.70)		
Item 3, Baseline (Day 1)	5.5 (± 1.02)	5.5 (± 0.91)		
Item 3, Month 6/5	0.0 (± 1.21)	-0.3 (± 1.42)		
Item 3, Month 12/11	0.0 (± 1.16)	-0.1 (± 1.38)		
Item 4, Baseline (Day 1)	5.2 (± 1.21)	5.2 (± 1.16)		
Item 4, Month 6/5	-0.1 (± 1.28)	0.4 (± 1.32)		
Item 4, Month 12/11	-0.2 (± 1.35)	0.3 (± 1.33)		
Item 5, Baseline (Day 1)	5.2 (± 1.16)	5.0 (± 1.24)		
Item 5, Month 6/5	-0.1 (± 1.30)	0.6 (± 1.42)		

Item 5, Month 12/11	-0.2 (± 1.33)	0.7 (± 1.43)		
Item 6, Baseline (Day 1)	4.9 (± 1.55)	4.7 (± 1.70)		
Item 6, Month 6/5	0.0 (± 1.58)	0.9 (± 1.77)		
Item 6, Month 12/11	-0.1 (± 1.58)	0.9 (± 1.74)		
Item 7, Baseline (Day 1)	5.5 (± 0.92)	5.5 (± 0.80)		
Item 7, Month 6/5	0.1 (± 0.75)	0.2 (± 0.81)		
Item 7, Month 12/11	0.1 (± 0.78)	0.1 (± 0.86)		
Item 8, Baseline (Day 1)	5.1 (± 1.11)	5.0 (± 1.20)		
Item 8, Month 6/5	-0.1 (± 1.26)	0.7 (± 1.36)		
Item 8, Month 12/11	-0.2 (± 1.38)	0.7 (± 1.31)		
Item 9, Baseline (Day 1)	5.5 (± 1.02)	5.5 (± 0.86)		
Item 9, Month 6/5	0.0 (± 1.09)	0.2 (± 1.10)		
Item 9, Month 12/11	-0.1 (± 1.04)	0.2 (± 1.04)		
Item 10, Baseline (Day 1)	4.9 (± 1.28)	4.9 (± 1.23)		
Item 10, Month 6/5	0.0 (± 1.38)	0.8 (± 1.54)		
Item 10, Month 12/11	-0.2 (± 1.45)	0.9 (± 1.49)		
Item 11, Baseline (Day 1)	5.3 (± 1.06)	5.2 (± 1.10)		
Item 11, Month 6/5	-0.2 (± 1.20)	0.5 (± 1.34)		
Item 11, Month 12/11	-0.3 (± 1.13)	0.5 (± 1.34)		
Item 12, Baseline (Day 1)	5.6 (± 0.94)	5.5 (± 1.02)		
Item 12, Month 6/5	-0.1 (± 0.93)	-0.6 (± 1.64)		
Item 12, Month 12/11	-0.2 (± 1.09)	-0.5 (± 1.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in total treatment satisfaction score using HIV treatment satisfaction status questionnaire (HIVTSQs) - mITT-E population

End point title	Change from baseline in total treatment satisfaction score using HIV treatment satisfaction status questionnaire (HIVTSQs) - mITT-E population[25]

End point description:

The HIVTSQs total treatment satisfaction score comprised of 11 items based on HIVTSQ questionnaire each graded on a scale of 0 (very dissatisfied) to 6 (very satisfied) which were summed to produce a total score range of 0-66. Higher scores represent greater treatment satisfaction. Baseline value is defined as latest pre-treatment assessment with a non-missing value, including those from unscheduled visits. Change from baseline is defined as post-dose visit value minus baseline value. For the Q2M arm, data from the Q2M OLI participants at Month 6 and 12 visit and Q2M D2I participants at Month 5 and 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 6 and 12 visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and up to Month 12

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	222	446		
Units: Scores on scale				
arithmetic mean (standard deviation)				
Baseline (Day 1)	58.38 (± 8.229)	57.88 (± 7.906)		
Month 6/5	-0.66 (± 7.417)	3.99 (± 9.670)		
Month 12/11	-1.93 (± 8.045)	4.21 (± 9.273)		

Statistical analyses

No statistical analyses for this end point

Secondary: Individual item scores of HIVTSQc at Month 12/11 - mITT-E population

End point title	Individual item scores of HIVTSQc at Month 12/11 - mITT-E population[26]

End point description:

Individual item scores were rated on a scale of +3 (much more satisfied', 'much more convenient', 'much more flexible') to -3 (much less satisfied', 'much less convenient', 'much less flexible'). Higher score indicates greater improvement, and lower score indicates greater deterioration in satisfaction with each aspect of treatment. A score of 0 represents no change. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

At Month 12/11

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	214	427		
Units: Scores on scale				
arithmetic mean (standard deviation)				
Item 1	1.60 (± 1.417)	2.56 (± 1.043)		
Item 2	1.88 (± 1.375)	2.47 (± 1.086)		
Item 3	1.63 (± 1.463)	2.10 (± 1.388)		
Item 4	1.42 (± 1.560)	2.41 (± 1.109)		
Item 5	1.38 (± 1.520)	2.50 (± 1.070)		
Item 6	1.24 (± 1.591)	2.41 (± 1.138)		
Item 7	1.94 (± 1.297)	2.35 (± 1.065)		
Item 8	1.43 (± 1.489)	2.56 (± 0.994)		
Item 9	1.73 (± 1.467)	2.61 (± 1.065)		

Item 10	1.22 (± 1.602)	2.58 (± 1.093)		
Item 11	1.43 (± 1.542)	2.46 (± 1.107)		
Item 12	1.64 (± 1.465)	1.85 (± 1.530)		

Statistical analyses

No statistical analyses for this end point

Secondary: HIV treatment satisfaction change questionnaire (HIVTSQc) total score at Month 12/11 - mITT-E population

End point title	HIV treatment satisfaction change questionnaire (HIVTSQc) total score at Month 12/11 - mITT-E population[27]

End point description:

HIV treatment satisfaction change questionnaire (HIVTSQc) total Score is computed with items 1-11 which were summed to produce a total score range of -33 to 33. Higher score indicated greater improvement in the satisfaction with the treatment and lower score indicated greater deterioration in treatment satisfaction. A score of 0 represents no change. For the Q2M arm, data from the Q2M OLI participants at Month 12 visit and Q2M D2I participants at Month 11 visit were combined as the study objective was to demonstrate the non-inferior antiviral activity of (Q2M) (OLI+ D2I combined) compared to BIK. For BIK arm, data was collected at month 12 visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

At Month 12/11

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Biktarvy (BIK)	Q2M (OLI + D2I)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	214	426		
Units: Scores on scale				
arithmetic mean (standard deviation)	16.89 (± 14.299)	26.97 (± 10.135)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from month 2/1 in dimension scores using perception of injection (PIN) questionnaire - Q2M - mITT-E population

End point title	Change from month 2/1 in dimension scores using perception of injection (PIN) questionnaire - Q2M - mITT-E population[28]

End point description:

The PIN questionnaire was used to explore the dimension scores based on 4 dimensions including acceptance of injection site reactions (ISRs), Bother from ISRs, Leg movement and Sleep categories. Domain scores were calculated as a mean of all items with the domain. The PIN response options range from 1 (totally acceptable) to 5 (not at all acceptable). This endpoint was only planned to be analyzed

for Q2M arm. Month 2/1 refers to the Month 2 (OLI and BIK) visit/Month 1 (DTI) visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

From Month 2/1 up to Month 12

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Oral lead-in phase (OLI)	Direct to injections (D2I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	271		
Units: Scores on scale				
arithmetic mean (standard deviation)				
Bother of ISRs, Month 2/1	1.58 (± 0.568)	1.60 (± 0.583)		
Bother of ISRs, Month 6/5	0.01 (± 0.528)	-0.03 (± 0.590)		
Bother of ISRs, Month 12/11	0.08 (± 0.594)	-0.04 (± 0.583)		
Leg Movement, Month 2/1	1.93 (± 1.013)	1.83 (± 0.913)		
Leg Movement, Month 6/5	-0.14 (± 0.779)	-0.22 (± 0.868)		
Leg Movement, Month 12/11	-0.18 (± 0.859)	-0.24 (± 0.817)		
Sleep, Month 2/1	1.83 (± 0.936)	1.87 (± 0.965)		
Sleep, Month 6/5	-0.01 (± 0.915)	-0.16 (± 0.869)		
Sleep, Month 12/11	-0.07 (± 0.948)	-0.17 (± 0.870)		
Acceptance, Month 2/1	2.02 (± 1.017)	2.05 (± 0.949)		
Acceptance, Month 6/5	-0.14 (± 0.906)	-0.13 (± 0.879)		
Acceptance, Month 12/11	-0.20 (± 0.873)	-0.26 (± 0.856)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from month 2/1 in individual item scores using PIN questionnaire- Q2M - mITT-E population

End point title	Change from month 2/1 in individual item scores using PIN questionnaire- Q2M - mITT-E population[29]

End point description:

The PIN questionnaire was used to explore the individual item scores based on anxiety before, pain, satisfaction, anxiety after and willingness categories. The items in the scale are rated on a 5-point scale and questions are phrased in such a way as to ensure that 1 is very dissatisfied and 5 was very satisfied. This endpoint was only planned to be analyzed for Q2M arm. Month 2/1 refers to the Month 2 (OLI and BIK) visit/Month 1 (DTI) visit. Month 6/5 refers to the Month 6 (OLI and BIK) visit/Month 5 (DTI) visit. Month 12/11 refers to the Month 12 (OLI and BIK) visit/Month 11 (DTI) visit.

End point type	Secondary

End point timeframe:

From Month 2/1 up to Month 12

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As per study design, the endpoints were presented for OLI + D2I arms combined as Q2M. Whereas, the baseline period was separated as OLI and D2I.

End point values	Oral lead-in phase (OLI)	Direct to injections (D2I)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	271		
Units: Scores on scale				
arithmetic mean (standard deviation)				
Anxiety Before, Month 2/1	1.9 (± 1.02)	1.9 (± 1.02)		
Anxiety Before, Month 6/5	-0.14 (± 1.021)	-0.22 (± 1.000)		
Anxiety Before, Month 12/11	-0.28 (± 0.973)	-0.22 (± 0.914)		
Pain, Month 2/1	1.8 (± 0.88)	2.0 (± 0.93)		
Pain, Month 6/5	0.09 (± 0.907)	-0.03 (± 0.935)		
Pain, Month 12/11	0.13 (± 0.995)	0.02 (± 0.943)		
Satisfaction, Month 2/1	1.7 (± 0.90)	1.6 (± 0.81)		
Satisfaction, Month 6/5	-0.06 (± 0.837)	0.00 (± 0.867)		
Satisfaction, Month 12/11	-0.12 (± 0.861)	-0.11 (± 0.830)		
Anxiety After, Month 2/1	1.8 (± 1.12)	1.7 (± 0.96)		
Anxiety After, Month 6/5	-0.14 (± 0.994)	-0.04 (± 0.916)		
Anxiety After, Month 12/11	-0.24 (± 0.947)	-0.16 (± 0.850)		
Willingness, Month 2/1	1.4 (± 0.76)	1.4 (± 0.78)		
Willingness, Month 6/5	0.01 (± 0.716)	-0.08 (± 0.794)		
Willingness, Month 12/11	-0.01 (± 0.744)	-0.10 (± 0.742)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality, non-serious adverse events (non-SAEs) and serious adverse events (SAEs) were collected maximum up to 12 months.

Adverse event reporting additional description:

Safety population included all randomly assigned participants who received at least one dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v24.1

Reporting groups

Reporting group title	Oral lead-in phase (OLI)

Reporting group description:

Participants with human immunodeficiency viruses (HIV)-1 who chose oral lead in (OLI) received oral 30 milligram (mg) Cabotegravir (CAB) tablet + 25 mg Rilpivirine (RPV) tablet once daily (QD) for one month. At the month 1 visit, the last dose of oral CAB + RPV was given, followed by the first 600 mg CAB long-acting (LA) + 900 mg RPV LA intramuscular injection (IM), and second injection of CAB LA 600 mg + RPV LA 900 mg at month 2, and then subsequent injections once every 2 months (Q2M) until Month 12.

Reporting group title	Biktarvy (BIK)

Reporting group description:

Participants with HIV-1 received BIK tablet orally until month 12. BIK was a fixed dose combination of 50 mg Bictegravir (BIC) + 200 mg Emtricitabine (FTC) + 25 mg Tenofovir alafenamide (TAF).

Reporting group title	Direct to injections (D2I)

Reporting group description:

Participants with HIV-1 who chose direct to injections (D2I) received the first injections of 600 mg CAB LA + 900 mg RPV LA, IM as initial loading doses at Day 1 one month, followed by second and third subsequent injections (CAB LA 600 mg + RPV LA 900 mg) at month 1 and month 3 followed by Q2M until Month 11.

Serious adverse events	Oral lead-in phase (OLI)	Biktarvy (BIK)	Direct to injections (D2I)
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 175 (6.29%)	15 / 227 (6.61%)	10 / 279 (3.58%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioblastoma multiforme			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			

subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injection site pain			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Substance abuse			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug abuse			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Device breakage			

subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 175 (1.14%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Contusion			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 175 (0.00%)	2 / 227 (0.88%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 175 (0.57%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhagic transformation stroke			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Brain injury			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Syncope			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anorectal disorder			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bursitis			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex meningoencephalitis			

subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex meningitis			
subjects affected / exposed	1 / 175 (0.57%)	0 / 227 (0.00%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 175 (0.00%)	0 / 227 (0.00%)	1 / 279 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Obesity			
subjects affected / exposed	0 / 175 (0.00%)	1 / 227 (0.44%)	0 / 279 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Oral lead-in phase (OLI)	Biktarvy (BIK)	Direct to injections (D2I)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 175 (74.29%)	77 / 227 (33.92%)	217 / 279 (77.78%)
Nervous system disorders			
Headache			
subjects affected / exposed	16 / 175 (9.14%)	12 / 227 (5.29%)	33 / 279 (11.83%)
occurrences (all)	17	12	43
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	104 / 175 (59.43%)	1 / 227 (0.44%)	178 / 279 (63.80%)
occurrences (all)	506	2	887
Injection site nodule			
subjects affected / exposed	17 / 175 (9.71%)	0 / 227 (0.00%)	25 / 279 (8.96%)
occurrences (all)	28	0	56
Injection site swelling			
subjects affected / exposed	14 / 175 (8.00%)	0 / 227 (0.00%)	26 / 279 (9.32%)
occurrences (all)	40	0	43
Pyrexia			
subjects affected / exposed	10 / 175 (5.71%)	8 / 227 (3.52%)	22 / 279 (7.89%)
occurrences (all)	14	8	32
Injection site discomfort			
subjects affected / exposed	15 / 175 (8.57%)	0 / 227 (0.00%)	24 / 279 (8.60%)
occurrences (all)	56	0	65
Injection site induration			
subjects affected / exposed	17 / 175 (9.71%)	0 / 227 (0.00%)	16 / 279 (5.73%)
occurrences (all)	42	0	33
Fatigue			
subjects affected / exposed	16 / 175 (9.14%)	6 / 227 (2.64%)	14 / 279 (5.02%)
occurrences (all)	19	7	18
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 175 (4.57%)	9 / 227 (3.96%)	19 / 279 (6.81%)
occurrences (all)	11	9	19
Infections and infestations			
COVID-19			

subjects affected / exposed	32 / 175 (18.29%)	38 / 227 (16.74%)	41 / 279 (14.70%)
occurrences (all)	33	38	43
Nasopharyngitis			
subjects affected / exposed	8 / 175 (4.57%)	10 / 227 (4.41%)	18 / 279 (6.45%)
occurrences (all)	11	13	22
Syphilis			
subjects affected / exposed	8 / 175 (4.57%)	9 / 227 (3.96%)	19 / 279 (6.81%)
occurrences (all)	9	10	19

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2020	The primary reason for protocol amendment 01 is to add minor clarifications to address study completion, PK collection, and endpoint timings. Country-specific details were added to Appendix 10 to address UK MHRA requirements. The protocol short title was updated. Corrections to typographical errors in protocol text and title were made throughout.
08 September 2021	The primary reason for protocol amendment 02 is to address and clarify comments raised during the course of the study and to implement country specific changes following regulatory review.
10 February 2022	The primary reason for protocol amendment 03 is to address and clarify comments raised during the course of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported