Clinical trial results:
A Phase IIb, randomized, partially blind, active controlled, dose-range finding study of GSK3640254 compared to a reference arm of dolutegravir, each in combination with nucleoside reverse transcriptase inhibitors, in HIV-1 infected antiretroviral treatment-naive adults

Summary

EudraCT number	2019-004435-23
Trial protocol	PT FR DE IT
Global end of trial date	29 May 2023

Results information

Result version number	v3 (current)
This version publication date	14 June 2024
First version publication date	21 September 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	208379

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04493216
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	21 October 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 September 2022
Global end of trial reached?	Yes
Global end of trial date	29 May 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate antiviral efficacy of GSK3640254 relative to DTG, each given in combination with 2 NRTIs, enabling the selection of an optimal dose for GSK3640254

Protection of trial subjects:

Not Applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 November 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 36
Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Portugal: 8
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	South Africa: 16
Country: Number of subjects enrolled	Spain: 41
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	161
EEA total number of subjects	68

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	160
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was terminated by the sponsor at Week 48 as the sponsor determined further development of GSK3640254-containing daily oral regimen would not be differentiated enough from existing 2-drug daily oral regimens. Thus, secondary analyses at Week 96 and Week 144 were not evaluated.

Pre-assignment

Screening details:

The changes from the planned subsequent analyses were presented as pre-specified in Statistical Analysis Plan. Safety analysis is presented based on the Entire Duration of Treatment Exposure period, which was defined from Day 1 up to end of continued access to treatment post-study termination (Day 922).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF

Arm description:

Participants with human immunodeficiency virus type 1 (HIV-1), orally received one 100 mg tablet per day of GSK3640254 and two tablets per day of matching placebo in a blinded setting. Open label dual nucleoside reverse transcriptase inhibitors (NRTIs) background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

Arm type	Experimental
Investigational medicinal product name	ABC/3TC or FTC/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open label dual NRTI background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

Investigational medicinal product name	100 mg GSK3640254
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants with human immunodeficiency virus type 1 (HIV-1) infected antiretroviral treatment-naive adults orally received one 100 mg tablet per day of GSK3640254 and two tablets per day of matching placebo as blinded.

Arm title	GSK3640254 150 mg + ABC/3TC or FTC/TAF

Arm description:

Participants with HIV-1, orally received 150 mg (one 100 mg tablet + two 25 mg tablets per day) of GSK3640254 in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Arm type	Experimental

Investigational medicinal product name	ABC/3TC or FTC/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open label dual NRTI background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

Investigational medicinal product name	150 mg GSK3640254
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants with HIV-1 infected antiretroviral treatment-naive adults orally received 150 mg (one 100 mg tablet + two 25 mg tablets per day) of GSK3640254 as blinded.

Arm title	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF

Arm description:

Participants with HIV-1, orally received two 100 mg tablets (200 mg) per day of GSK3640254 and one tablet per day of matching placebo in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Arm type	Experimental
Investigational medicinal product name	ABC/3TC or FTC/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open label dual NRTI background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

Investigational medicinal product name	200 mg GSK3640254
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants with HIV-1 infected antiretroviral treatment-naive adults orally received two 100 mg tablets (200 mg) per day of GSK3640254 and one tablet per day of matching placebo as blinded.

Arm title	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF

Arm description:

Participants with HIV-1, orally received one 50 mg tablet per day of DTG in an open label setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Arm type	Active comparator
Investigational medicinal product name	ABC/3TC or FTC/TAF
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Open label dual NRTI background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

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

Dosage and administration details:

Participants with HIV-1 infected antiretroviral treatment-naive adults orally received one 50 mg tablet per day of DTG in an open label setting.

Number of subjects in period 1	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Started	40	43	42
Completed	0	0	0
Not completed	40	43	42
Consent withdrawn by subject	2	1	1
Physician decision	-	-	1
Subject reached protocol-defined stopping criteria	4	2	7
Adverse event, non-fatal	1	4	5
Study terminated by sponsor	30	33	28
Lost to follow-up	2	1	-
Protocol deviation	1	2	-

Number of subjects in period 1	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Started	36
Completed	0
Not completed	36
Consent withdrawn by subject	2
Physician decision	-
Subject reached protocol-defined stopping criteria	2
Adverse event, non-fatal	2
Study terminated by sponsor	27
Lost to follow-up	1
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF
Reporting group description:	
Participants with human immunodeficiency virus type 1 (HIV-1), orally received one 100 mg tablet per day of GSK3640254 and two tablets per day of matching placebo in a blinded setting. Open label dual nucleoside reverse transcriptase inhibitors (NRTIs) background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.	
Reporting group title	GSK3640254 150 mg + ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received 150 mg (one 100 mg tablet + two 25 mg tablets per day) of GSK3640254 in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	
Reporting group title	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received two 100 mg tablets (200 mg) per day of GSK3640254 and one tablet per day of matching placebo in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	
Reporting group title	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received one 50 mg tablet per day of DTG in an open label setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	

Reporting group values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Number of subjects	40	43	42
Age categorical Units: Subjects			
19-64 years	40	42	42
>=65 years	0	1	0
Sex: Female, Male Units: Participants			
Female	7	9	12
Male	33	34	30
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	1	2	1
ASIAN	0	2	2
BLACK OR AFRICAN AMERICAN	6	8	6
WHITE	32	31	32
MIXED RACE	1	0	0
MISSING	0	0	1
Age, Continuous Units: YEARS			
arithmetic mean	32.8	38.1	33.7
standard deviation	± 6.20	± 12.54	± 10.59

Reporting group values	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF	Total	
Number of subjects	36	161	
Age categorical Units: Subjects			
19-64 years	36	160	
>=65 years	0	1	
Sex: Female, Male Units: Participants			
Female	10	38	
Male	26	123	
Race/Ethnicity, Customized Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	4	
ASIAN	1	5	
BLACK OR AFRICAN AMERICAN	6	26	
WHITE	29	124	
MIXED RACE	0	1	
MISSING	0	1	
Age, Continuous Units: YEARS			
arithmetic mean	35.3		
standard deviation	± 9.85	-	

End points

End points reporting groups

Reporting group title	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF
Reporting group description:	
Participants with human immunodeficiency virus type 1 (HIV-1), orally received one 100 mg tablet per day of GSK3640254 and two tablets per day of matching placebo in a blinded setting. Open label dual nucleoside reverse transcriptase inhibitors (NRTIs) background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.	
Reporting group title	GSK3640254 150 mg + ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received 150 mg (one 100 mg tablet + two 25 mg tablets per day) of GSK3640254 in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	
Reporting group title	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received two 100 mg tablets (200 mg) per day of GSK3640254 and one tablet per day of matching placebo in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	
Reporting group title	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Reporting group description:	
Participants with HIV-1, orally received one 50 mg tablet per day of DTG in an open label setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.	

Primary: Percentage of participants with plasma HIV-1 ribonucleic acid (RNA) less than (<)50 copies per milliliter (c/mL) at Week 24

End point title	Percentage of participants with plasma HIV-1 ribonucleic acid (RNA) less than (<)50 copies per milliliter (c/mL) at Week 24
End point description:	
Percentage of participants with plasma HIV-1 RNA <50 c/mL at week 24 was assessed using the Food and Drug Administration (FDA) snapshot algorithm to demonstrate the antiviral activity of GSK3640254 given in combination with either ABC/3TC or FTC/TAF compared to the reference treatment of DTG given in combination with either ABC/3TC or FTC/TAF. The analysis was performed on the Intent-to-Treat Exposed (ITT-E) population which included all randomized participants who received at least one dose of study intervention.	
End point type	Primary
End point timeframe:	
At Week 24	

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Percentage of participants				
number (confidence interval 95%)	82.5 (68.1 to 91.3)	90.7 (78.4 to 96.3)	76.2 (61.5 to 86.5)	91.7 (78.2 to 97.1)

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Differences in percentage of participant = Percentage of participant in GSK3640254 150 mg+ ABC/3TC or FTC/TAF - Percentage of participant in DTG+ ABC/3TC or FTC/TAF	
Comparison groups	GSK3640254 150 mg + ABC/3TC or FTC/TAF v Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Number of subjects included in analysis	79
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Differences in percentage of participant
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.5
upper limit	11.6

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Differences in percentage of participant = Percentage of participant in GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF - Percentage of participant in DTG+ABC/3TC or FTC/TAF	
Comparison groups	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF v Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Differences in percentage of participant
Point estimate	-9.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24
upper limit	5.7

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Differences in percentage of participant = Percentage of participant in GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF - Percentage of participant in DTG+ ABC/3TC or FTC/TAF	
Comparison groups	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF v Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF

Number of subjects included in analysis	78
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Differences in percentage of participant
Point estimate	-15.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.2
upper limit	0.3

Secondary: Absolute values of HIV-1 RNA at Weeks 24 and 48

End point title	Absolute values of HIV-1 RNA at Weeks 24 and 48

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 have been presented. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. The analysis was performed on the ITT-E population which included all randomized participants who received at least one dose of study intervention. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Log 10 copies per milliliter				
arithmetic mean (standard deviation)				
Baseline (Day 1)	4.351 (± 0.5712)	4.353 (± 0.6705)	4.165 (± 0.6505)	4.247 (± 0.6765)
Week 24	1.619 (± 0.1260)	1.607 (± 0.0663)	1.610 (± 0.0679)	1.592 (± 0.0126)
Week 48	1.602 (± 0.0536)	1.605 (± 0.0647)	1.594 (± 0.0233)	1.590 (± 0.0000)

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Percentage of participants with plasma HIV-1 RNA <50 c/mL at week 48 was assessed using the FDA snapshot algorithm to demonstrate the antiviral activity of GSK3640254 given in combination with either ABC/3TC or FTC/TAF compared to the reference treatment of DTG given in combination with either ABC/3TC or FTC/TAF. The analysis was performed on the ITT-E population which included all randomized participants who received at least one dose of study intervention.

End point type	Secondary

End point timeframe:

At Week 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Percentage of participants				
number (confidence interval 95%)	85.0 (70.9 to 92.9)	83.7 (70.0 to 91.9)	76.2 (61.5 to 86.5)	77.8 (61.9 to 88.3)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in plasma HIV-1 RNA at Weeks 24 and 48

End point title	Change from Baseline in plasma HIV-1 RNA at Weeks 24 and 48

End point description:

Plasma samples were collected for quantitative analysis of HIV-1 RNA. log10 values for plasma HIV-1 RNA have been presented. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. The analysis was performed on the ITT-E population which included all randomized participants who received at least one dose of study intervention. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Log 10 copies per milliliter				
arithmetic mean (standard deviation)				

Baseline (Day 1)	4.351 (± 0.5712)	4.353 (± 0.6705)	4.165 (± 0.6505)	4.247 (± 0.6765)
Change from Baseline to Week 24	-2.718 (± 0.5501)	-2.784 (± 0.6615)	-2.565 (± 0.6513)	-2.629 (± 0.6835)
Change from Baseline to Week 48	-2.675 (± 0.5640)	-2.762 (± 0.6784)	-2.580 (± 0.6941)	-2.717 (± 0.6672)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of Cluster of differentiation 4 plus (CD4+) cell counts at Weeks 24 and 48

End point title	Absolute values of Cluster of differentiation 4 plus (CD4+) cell counts at Weeks 24 and 48

End point description:

Blood samples were collected and CD4+ cell count was assessed using flow cytometry. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. The analysis was performed on the ITT-E population which included all randomized participants who received at least one dose of study intervention. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
Baseline (Day 1)	480.3 (± 171.72)	509.7 (± 207.13)	478.7 (± 204.04)	514.1 (± 240.88)
Week 24	717.5 (± 222.91)	643.5 (± 202.27)	689.8 (± 316.64)	724.8 (± 403.99)
Week 48	749.9 (± 328.28)	702.6 (± 258.65)	747.3 (± 313.15)	705.2 (± 221.18)

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Blood samples were collected and CD4+ cell count was assessed using flow cytometry. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. Change from Baseline is defined as post-dose visit value minus Baseline value. The analysis was performed on the ITT-E population which included all randomized participants who received at least one dose of study intervention. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Cells per cubic millimeter				
arithmetic mean (standard deviation)				
Baseline (Day 1)	480.3 (± 171.72)	509.7 (± 207.13)	478.7 (± 204.04)	514.1 (± 240.88)
Change from Baseline to Week 24	241.3 (± 191.26)	129.3 (± 233.07)	202.3 (± 271.98)	198.5 (± 285.00)
Change from Baseline to Week 48	292.4 (± 264.16)	189.2 (± 216.10)	243.0 (± 233.24)	190.6 (± 180.19)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with serious adverse events (SAEs) and deaths

End point title	Number of participants with serious adverse events (SAEs) and deaths

End point description:

An SAE was defined as any serious adverse event that, at any dose resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or any other situation according to medical or scientific judgment. The analysis was performed on the Safety Population, which included all randomized participants who were exposed to study intervention with the exception of any participants with documented evidence of not having consumed any amount of study intervention.

End point type	Secondary

End point timeframe:

From Day 1 up to end of continued access to treatment post-study termination (Day 922)

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Participants				
Serious Adverse Events	2	7	2	2
Deaths	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) leading to treatment discontinuation

End point title	Number of participants with adverse events (AEs) leading to treatment discontinuation

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Number of participants who discontinued study treatment due to AEs are presented. The analysis was performed on the Safety Population, which included all randomized participants who were exposed to study intervention with the exception of any participants with documented evidence of not having consumed any amount of study intervention.

End point type	Secondary

End point timeframe:

From Day 1 up to end of continued access to treatment post-study termination (Day 922)

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Participants				
AEs leading to treatment discontinuation	2	4	5	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AE based on maximum severity grades

End point title	Number of participants with AE based on maximum severity grades

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. The severity of AEs was defined as per the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events and was categorized into grades: Grade 1 - mild, Grade 2 - moderate, Grade 3 - severe, Grade 4 - Potentially life threatening, Grade 5 - Fatal. The analysis was performed on the Safety Population, which included all randomized participants who were exposed to study intervention except for any participants with documented evidence of not having consumed any amount of study intervention. The data presented here is not cumulative data but the number of participants experiencing the adverse event based on maximum grade at the indicated timepoints.

End point type	Secondary

End point timeframe:

From Day 1 up to end of continued access to treatment post-study termination (Day 922)

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Participants				
Grade 1	12	14	17	15
Grade 2	19	17	17	10
Grade 3	5	5	3	3
Grade 4	1	2	1	0
Grade 5	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with AEs of special interest (AESI)

End point title	Number of participants with AEs of special interest (AESI)

End point description:

An AE was any untoward medical occurrence in a clinical study participant, temporally associated with the use of a study intervention, whether or not considered related to the study intervention. Number of participants with AESI in (gastrointestinal (GI), nervous system, and psychiatric AEs) are presented. The analysis was performed on the Safety Population, which included all randomized participants who were exposed to study intervention with the exception of any participants with documented evidence of not having consumed any amount of study intervention.

End point type	Secondary

End point timeframe:

From Day 1 up to end of continued access to treatment post-study termination (Day 922)

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	43	42	36
Units: Participants				
AESI (Gastrointestinal)	15	18	14	14
AESI (Nervous system)	7	5	7	3
AESI (Psychiatric)	4	3	4	4

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with genotypic resistance

End point title	Number of participants with genotypic resistance

End point description:

Plasma samples were collected for resistance testing. Genotypic testing was conducted in participants meeting protocol-defined virologic failure (PDVF) criteria. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. The analysis was performed on the PDVF Population, which included participants with A. virologic non-response (Decrease from Baseline [Day 1] in plasma HIV-1 RNA of 1.0 log10 c/mL unless plasma HIV-1 RNA is <200 c/mL by Week 12; confirmed plasma HIV-1 RNA levels ≥200 c/mL at or after Week 24; plasma HIV-1 RNA ≥50 c/mL on repeat testing of Week 24 results and prior to Week 28) and B. virologic rebound (confirmed plasma HIV-1 RNA ≥200 c/mL after confirmed consecutive plasma HIV-1 RNA <50 c/mL).

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	5	1
Units: Participants				
Baseline (Day 1)	0	0	0	0
Weeks 24	0	0	0	0
Weeks 48	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Observed plasma concentration at the end of the dosing interval (Ctau)

of GSK3640254 at steady state - Week 2

End point title	Observed plasma concentration at the end of the dosing interval (Ctau) of GSK3640254 at steady state - Week 2[1]

End point description:

Blood samples were collected at indicated time points for pharmacokinetic (PK) analysis of GSK3640254. Observed plasma concentration at the end of the dosing interval was determined directly from the concentration-time data. The analysis was performed on the Intensive PK Population, which included all participants who received at least one dose of GSK3640254, had evaluable drug concentrations reported and where samples were collected according to the intensive PK sampling scheme. Only those participants who received GSK3640254 have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	18	
Units: Nanogram/ milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Week 2	430.5361 (± 56.5)	604.8387 (± 44.2)	805.2209 (± 43.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with phenotypic resistance

End point title	Number of participants with phenotypic resistance

End point description:

Plasma samples were collected to for resistance testing. Phenotypic testing was conducted in participants meeting PDVF criteria. Baseline was defined as the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. The analysis was performed on the PDVF Population. Only those participants with data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Baseline (Day 1) and at Weeks 24 and 48

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	2	5	1
Units: Participants				
Baseline (Day 1)	0	0	0	0
Weeks 24	0	0	0	0
Weeks 48	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Observed plasma concentration at the end of the dosing interval (Ctau) of GSK3640254 at steady state - Week 24 and 48

End point title	Observed plasma concentration at the end of the dosing interval (Ctau) of GSK3640254 at steady state - Week 24 and 48[2]

End point description:

Blood samples were collected at indicated time points for pharmacokinetic (PK) analysis of GSK3640254. Observed plasma concentration at the end of the dosing interval was determined directly from the concentration-time data. The analysis was performed on the Sparse PK Population, which included all participants who received at least one dose of GSK3640254, had evaluable drug concentrations reported and had samples collected according to the sparse PK sampling scheme. Only those participants who received GSK3640254 and had data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

At Weeks 24 and 48

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	12	10	13	
Units: Nanogram/ milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Week 24	396.5117 (± 62.5)	519.6041 (± 84.9)	922.9638 (± 51.6)	
Week 48	310.9877 (± 135.4)	568.0656 (± 13.4)	812.4745 (± 49.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval (AUC [0-tau]) of GSK3640254 at steady state

End point title	Area under the plasma drug concentration-time curve from pre-dose to the end of the dosing interval (AUC [0-tau]) of GSK3640254 at steady state[3]

End point description:

Blood samples were collected at indicated time points for PK analysis of GSK3640254. The analysis was performed on the Intensive PK Population. Only those participants who received GSK3640254 and had data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	18	
Units: Hour*nanogram/ milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)	14995.7576 (± 49.8)	21212.2480 (± 44.5)	30708.2546 (± 40.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed concentration (Cmax) of GSK3640254 at steady state

End point title	Maximum observed concentration (Cmax) of GSK3640254 at steady state[4]

End point description:

Blood samples were collected at indicated time points for PK analysis of GSK3640254. The analysis was performed on the Intensive PK Population. Only those participants who received GSK3640254 have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	18	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	929.8 (± 45.9)	1337.3 (± 47.7)	2094.5 (± 39.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Observed pre-dose plasma concentration (C0) of GSK3640254 at steady state

End point title	Observed pre-dose plasma concentration (C0) of GSK3640254 at steady state[5]

End point description:

Blood samples were collected at indicated time points for PK analysis of GSK3640254. Observed pre-dose plasma concentration was determined directly from the concentration-time data. The analysis was performed on the Intensive PK Population. Only those participants who received GSK3640254 have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	18	
Units: ng/mL				
geometric mean (geometric coefficient of variation)	435.9 (± 54.6)	603.2 (± 59.5)	865.2 (± 43.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Steady state oral clearance (CLt/F) of GSK3640254

End point title	Steady state oral clearance (CLt/F) of GSK3640254[6]

End point description:

Blood samples were collected at indicated time points for PK analysis of GSK3640254. The analysis was performed on the Intensive PK Population. Only those participants who received GSK3640254 and had

data available at specified time points have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	13	18	
Units: Liter/ hour				
geometric mean (geometric coefficient of variation)	6.6686 (± 49.8)	7.0714 (± 44.5)	6.5129 (± 40.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Cmax (Tmax) of GSK3640254 at steady state

End point title	Time to Cmax (Tmax) of GSK3640254 at steady state[7]

End point description:

Blood samples were collected at indicated time points for PK analysis of GSK3640254. Tmax was determined directly from the concentration-time data. The analysis was performed on the Intensive PK Population. Only those participants who received GSK3640254 have been analyzed.

End point type	Secondary

End point timeframe:

Pre-dose, 1, 2, 3, 3.5, 4, 4.5, 5, 6, 10, and 24 hours post-dose at Week 2

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 objective of this endpoint, only analysis of GSK3640254 was planned to present.

End point values	GSK3640254 100 mg+ Placebo+ ABC/3TC or FTC/TAF	GSK3640254 150 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	15	13	18	
Units: Hour				
median (full range (min-max))	3.0000 (1.900 to 9.017)	3.4167 (1.000 to 9.000)	3.4583 (1.917 to 5.000)	

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 from Day 1 up to end of continued access to treatment post-study termination (Day 922).

Adverse event reporting additional description:

The study was terminated by the sponsor after primary analysis (at week 48). As prespecified in Statistical analysis plan, AEs were collected up to end of continued access to treatment post-study termination (Day 922).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	GSK3640254 100 milligram(mg)+ Placebo+ ABC/3TC or FTC/TAF

Reporting group description:

Participants with human immunodeficiency virus type 1 (HIV-1), orally received one 100 mg tablet per day of GSK3640254 and two tablets per day of matching placebo in a blinded setting. Open label dual nucleoside reverse transcriptase inhibitors (NRTIs) background therapies were given as one tablet per day of 600 mg abacavir (ABC) / 300 mg lamivudine (3TC) OR 200 mg emtricitabine (FTC) / 25 mg tenofovir alafenamide (TAF) orally.

Reporting group title	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF

Reporting group description:

Participants with HIV-1, orally received one 50 mg tablet per day of DTG in an open label setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Reporting group title	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF

Reporting group description:

Participants with HIV-1, orally received two 100 mg tablets (200 mg) per day of GSK3640254 and one tablet per day of matching placebo in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Reporting group title	GSK3640254 150 mg + ABC/3TC or FTC/TAF

Reporting group description:

Participants with HIV-1, orally received 150 mg (one 100 mg tablet + two 25 mg tablets per day) of GSK3640254 in a blinded setting. Open label dual NRTI background therapies were given as one tablet per day combination of 600 mg ABC / 300 mg 3TC OR 200 mg FTC / 25 mg TAF orally.

Serious adverse events	GSK3640254 100 milligram(mg)+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)	2 / 36 (5.56%)	2 / 42 (4.76%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			

subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	0 / 42 (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
Pancreatitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	0 / 42 (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
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			

subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Substance dependence			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	0 / 42 (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
Suicidal ideation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	0 / 42 (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
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 36 (2.78%)	0 / 42 (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
Necrotising fasciitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	GSK3640254 150 mg + ABC/3TC or FTC/TAF		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 43 (16.28%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Limb fracture			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary hypertension			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Substance dependence			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Cellulitis			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Necrotising fasciitis			

subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	GSK3640254 100 milligram(mg)+ Placebo+ ABC/3TC or FTC/TAF	Dolutegravir (DTG) 50 mg + ABC/3TC or FTC/TAF	GSK3640254 200 mg+ Placebo+ ABC/3TC or FTC/TAF
Total subjects affected by non-serious adverse events			
subjects affected / exposed	37 / 40 (92.50%)	28 / 36 (77.78%)	38 / 42 (90.48%)
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	3 / 40 (7.50%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	3	1	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	1	0	1
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	2	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	2	1	3
Headache			

subjects affected / exposed	6 / 40 (15.00%)	3 / 36 (8.33%)	7 / 42 (16.67%)
occurrences (all)	6	4	10
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 40 (10.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	5	1	1
Asthenia			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	3 / 42 (7.14%)
occurrences (all)	2	2	3
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	2	1	1
Dyspepsia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	1	1	3
Diarrhoea			
subjects affected / exposed	5 / 40 (12.50%)	9 / 36 (25.00%)	6 / 42 (14.29%)
occurrences (all)	5	10	7
Abdominal pain upper			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	3 / 42 (7.14%)
occurrences (all)	1	3	3
Abdominal pain			
subjects affected / exposed	2 / 40 (5.00%)	2 / 36 (5.56%)	3 / 42 (7.14%)
occurrences (all)	2	2	3
Vomiting			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	0 / 42 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	2 / 42 (4.76%)
occurrences (all)	0	2	2
Nausea			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	3 / 42 (7.14%)
occurrences (all)	2	1	3
Haemorrhoids			

subjects affected / exposed	0 / 40 (0.00%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	3 / 40 (7.50%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	3	1	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 40 (5.00%)	3 / 36 (8.33%)	2 / 42 (4.76%)
occurrences (all)	2	4	2
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 40 (2.50%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	1	3	1
Infections and infestations			
COVID-19			
subjects affected / exposed	10 / 40 (25.00%)	10 / 36 (27.78%)	6 / 42 (14.29%)
occurrences (all)	12	13	7
Chlamydial infection			
subjects affected / exposed	2 / 40 (5.00%)	1 / 36 (2.78%)	1 / 42 (2.38%)
occurrences (all)	2	1	2
Gastroenteritis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 36 (0.00%)	2 / 42 (4.76%)
occurrences (all)	1	0	2
Gonorrhoea			
subjects affected / exposed	2 / 40 (5.00%)	0 / 36 (0.00%)	2 / 42 (4.76%)
occurrences (all)	2	0	2
Influenza			
subjects affected / exposed	3 / 40 (7.50%)	4 / 36 (11.11%)	3 / 42 (7.14%)
occurrences (all)	3	5	3
Respiratory tract infection			
subjects affected / exposed	3 / 40 (7.50%)	0 / 36 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Pharyngitis			
subjects affected / exposed	4 / 40 (10.00%)	3 / 36 (8.33%)	1 / 42 (2.38%)
occurrences (all)	4	3	1

Nasopharyngitis			
subjects affected / exposed	4 / 40 (10.00%)	3 / 36 (8.33%)	3 / 42 (7.14%)
occurrences (all)	5	6	5
Monkeypox			
subjects affected / exposed	1 / 40 (2.50%)	1 / 36 (2.78%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
Syphilis			
subjects affected / exposed	3 / 40 (7.50%)	5 / 36 (13.89%)	3 / 42 (7.14%)
occurrences (all)	3	6	3
Upper respiratory tract infection			
subjects affected / exposed	4 / 40 (10.00%)	1 / 36 (2.78%)	3 / 42 (7.14%)
occurrences (all)	5	1	5
Urethritis			
subjects affected / exposed	1 / 40 (2.50%)	2 / 36 (5.56%)	0 / 42 (0.00%)
occurrences (all)	1	2	0

Non-serious adverse events	GSK3640254 150 mg + ABC/3TC or FTC/TAF		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 43 (88.37%)		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Nervous system disorders			

Dizziness			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
Asthenia			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Food poisoning			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	7 / 43 (16.28%)		
occurrences (all)	8		
Abdominal pain upper			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Toothache			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	3		
Nausea			

subjects affected / exposed	6 / 43 (13.95%)		
occurrences (all)	8		
Haemorrhoids			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Rhinitis allergic			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	3		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Infections and infestations			
COVID-19			
subjects affected / exposed	12 / 43 (27.91%)		
occurrences (all)	12		
Chlamydial infection			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Gonorrhoea			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Influenza			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	4		
Respiratory tract infection			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		

Pharyngitis subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 5		
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 4		
Monkeypox subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Syphilis subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 3		
Urethritis subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 September 2020	This is a global amendment and was created primarily to replace details of the internal Safety Review Committee to reflect the use instead of an Independent Data Monitoring Committee (IDMC). The decision to switch was based on feedback received from several health authorities and ethics committees, with advice and approval by VH guidance committee. This amendment also includes corrections, clarifications and minor administrative errors. In addition, details from 2 prior country-specific amendments (Canada amendment CAN-1 and Portugal amendment POR-1) were incorporated into this global amendment.
09 April 2021	This is a global amendment. This amendment was created primarily to make non-substantial changes generally related to inclusion/exclusion criteria and the screening period, esophagogastroduodenoscopy (EGD) biopsy-based stopping criteria for individual participants and the study overall. The other changes exist for further detail, clarity, and current information.
10 May 2021	Study 208379 is undergoing this substantial amendment to reduce the sample size from approximately 210 participants to approximately 150 participants. This reduction of 60 participants will occur equally among the 3 experimental arms. There is no change to the Dolutegravir (DTG) reference arm. Thus, the number of participants will be as follows (each arm in combination with open-label Nucleoside Reverse Transcriptase Inhibitor [NRTI] backbone as originally described):

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported