Clinical trial results:
Phase IIb, randomized, double-blind, parallel-group study to assess the efficacy, safety, tolerability, and resistance profile of GSK3640254 in combination with dolutegravir compared to dolutegravir plus lamivudine in HIV-1 infected, treatment naïve adults

Summary

EudraCT number	2021-000016-28
Trial protocol	FR DE PT ES IT
Global end of trial date	11 May 2023

Results information

Result version number	v1 (current)
This version publication date	16 February 2024
First version publication date	16 February 2024

Trial information

Trial identification

Sponsor protocol code	212483

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	ViiV Healthcare
Sponsor organisation address	980 GreatWest Road, Brentford,Middlesex, United Kingdom, TW8 9GS
Public contact	ViiV Healthcare, GSK Response Center, 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	Final
Date of interim/final analysis	07 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate antiviral efficacy of GSK3640254 (all concentrations)+ DTG, relative to DTG+3TC at week 24 in HIV-1 infected ART (anti-retroviral therapy) naive participants.

Protection of trial subjects:

Not applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2021
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: 8
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Puerto Rico: 8
Country: Number of subjects enrolled	South Africa: 7
Country: Number of subjects enrolled	Spain: 36
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	85
EEA total number of subjects	50

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

Subject disposition

Recruitment

Recruitment details:

This study assessed efficacy, safety and resistance of GSK3640254 in combination with dolutegravir (DTG) compared to DTG+lamivudine in HIV-1 infected treatment-naïve adults. Study was terminated after primary analysis as the sponsor determined further development of study regimen would not be differentiated enough from existing similar regimens.

Pre-assignment

Screening details:

The changes from the planned subsequent analyses were presented as pre-specified in Statistical Analysis Plan. Secondary analyses at week 48 were not evaluated. Safety analysis is presented based on the Entire Duration of Treatment Exposure period, defined as from Day 1 up to end of continued access to treatment post-study termination (Day 478).

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, Monitor, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg

Arm description:

Participants with human immunodeficiency virus type 1 (HIV-1) orally received low dose (100 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir (50 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 50 mg tablet administered daily via oral administration

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

Dosage and administration details:

One or more tablets (equivalent of 100 mg product) administered daily via oral administration

Arm title	GSK3640254 150 mg + DTG 50 mg

Arm description:

Participants with HIV-1 orally received medium dose (150 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Arm type	Experimental

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

Dosage and administration details:

One 50 mg tablet administered daily via oral administration

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

Dosage and administration details:

One or more tablets (equivalent of 150 mg product) administered daily via oral administration

Arm title	GSK3640254 200 mg + DTG 50 mg

Arm description:

Participants with HIV-1 orally received high dose (200 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Arm type	Experimental
Investigational medicinal product name	Dolutegravir (50 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One 50 mg tablet administered daily via oral administration

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

Dosage and administration details:

One or more tablets (equivalent of 200 mg product) administered daily via oral administration

Arm title	DTG 50 mg + Lamivudine (3TC) 300 mg

Arm description:

Participants with HIV-1 orally received unblinded 50 mg DTG one tablet and blinded 300 mg 3TC. Each participant received one capsule per day of each intervention up to Week 24.

Arm type	Active comparator
Investigational medicinal product name	Lamivudine (300 mg)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 300 mg capsule administered daily via oral administration

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

Dosage and administration details:

One 50 mg tablet administered daily via oral administration

Number of subjects in period 1	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg
Started	22	20	22
Completed	2	3	2
Not completed	20	17	20
Consent withdrawn by subject	-	1	-
Protocol-defined stoping criteria reached	-	-	2
Adverse event, non-fatal	1	-	1
Protocol Deviation	1	1	-
Study terminated by sponsor	18	15	17
Lost to follow-up	-	-	-

Number of subjects in period 1	DTG 50 mg + Lamivudine (3TC) 300 mg
Started	21
Completed	3
Not completed	18
Consent withdrawn by subject	-
Protocol-defined stoping criteria reached	2
Adverse event, non-fatal	1
Protocol Deviation	-
Study terminated by sponsor	14
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg
Reporting group description:	
Participants with human immunodeficiency virus type 1 (HIV-1) orally received low dose (100 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	GSK3640254 150 mg + DTG 50 mg
Reporting group description:	
Participants with HIV-1 orally received medium dose (150 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	GSK3640254 200 mg + DTG 50 mg
Reporting group description:	
Participants with HIV-1 orally received high dose (200 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	DTG 50 mg + Lamivudine (3TC) 300 mg
Reporting group description:	
Participants with HIV-1 orally received unblinded 50 mg DTG one tablet and blinded 300 mg 3TC. Each participant received one capsule per day of each intervention up to Week 24.	

Reporting group values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg
Number of subjects	22	20	22
Age categorical Units: Subjects			
Adults (18-64 years)	22	20	22
Age Continuous Units: Years			
arithmetic mean	34.2	36.9	32.6
standard deviation	± 7.53	± 10.51	± 8.41
Sex: Female, Male Units: Participants			
Female	3	4	5
Male	19	16	17
Race/Ethnicity, Customized Units: Subjects			
Asian	0	0	0
Black or African American	3	4	3
White	18	14	16
Mixed Race	0	1	1
Other - Unspecified	1	1	2

Reporting group values	DTG 50 mg + Lamivudine (3TC) 300 mg	Total	
Number of subjects	21	85	
Age categorical Units: Subjects			
Adults (18-64 years)	21	85	

Age Continuous Units: Years			
arithmetic mean	32.1		
standard deviation	± 8.62	-	
Sex: Female, Male Units: Participants			
Female	3	15	
Male	18	70	
Race/Ethnicity, Customized Units: Subjects			
Asian	1	1	
Black or African American	3	13	
White	14	62	
Mixed Race	0	2	
Other - Unspecified	3	7	

End points

End points reporting groups

Reporting group title	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg
Reporting group description:	
Participants with human immunodeficiency virus type 1 (HIV-1) orally received low dose (100 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	GSK3640254 150 mg + DTG 50 mg
Reporting group description:	
Participants with HIV-1 orally received medium dose (150 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	GSK3640254 200 mg + DTG 50 mg
Reporting group description:	
Participants with HIV-1 orally received high dose (200 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.	
Reporting group title	DTG 50 mg + Lamivudine (3TC) 300 mg
Reporting group description:	
Participants with HIV-1 orally received unblinded 50 mg DTG one tablet and blinded 300 mg 3TC. Each participant received one capsule per day of each intervention up to Week 24.	

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[1]
End point description:	
Percentage of participants with plasma HIV-1 RNA <50 c/mL at Week 24 using the Food and Drug Administration (FDA) snapshot algorithm was assessed to evaluate the antiviral activity in HIV-1 infected ART (anti-retroviral therapy)-naïve participants. Analysis was performed on Intent-to-Treat Exposed (ITT-E) Population included all randomized participants who received at least one dose of study intervention and had data for plasma HIV-1 RNA <50 c/mL as per timeline assessed.	
End point type	Primary
End point timeframe:	
At Week 24	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: This endpoint was descriptive, hence no statistical analysis was performed.

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Percentage of participants	95	85	77	86

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of HIV-1 RNA through Week 24

End point title	Absolute values of HIV-1 RNA through Week 24

End point description:

Plasma samples were collected for quantitative analysis of HIV-1 RNA. Logarithm to base 10 (log 10) values for plasma HIV-1 RNA has been presented. Baseline is defined as the latest non-missing value prior to first dose of treatment according to date and time including unscheduled visits.
Analysis was performed on ITT-E Population that had data for absolute values of HIV-1 RNA as per timeline assessed.

End point type	Secondary

End point timeframe:

At Baseline (Day 1) and Week 24

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: log10 copies per milliliter(log10 c/mL)				
arithmetic mean (standard deviation)				
Baseline (Day 1) (N=22,20,22,21)	4.614 (± 0.5253)	4.446 (± 0.5913)	4.535 (± 0.4165)	4.179 (± 0.5907)
Week 24 (N=21,19,20,19)	1.315 (± 0.0737)	1.532 (± 0.7086)	1.349 (± 0.1431)	1.379 (± 0.2439)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in HIV-1 RNA through Week 24

End point title	Change from Baseline in HIV-1 RNA through Week 24

End point description:

Plasma samples were collected for quantitative analysis of HIV-1 RNA. Logarithm to base 10 (log 10) values for plasma HIV-1 RNA has been presented. Change from Baseline is defined as post-dose visit value minus Baseline value.
Analysis was performed on ITT-E Population that had data for absolute values of HIV-1 RNA as per timeline assessed.

End point type	Secondary

End point timeframe:

At Week 24 compared to baseline (Day 1)

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	20	19
Units: log10 c/mL				
arithmetic mean (standard deviation)	-3.306 (± 0.5163)	-2.874 (± 0.8476)	-3.186 (± 0.4809)	-2.767 (± 0.5531)

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute values of cluster of differentiation 4+ (CD4+) T-cell counts through Week 24

End point title	Absolute values of cluster of differentiation 4+ (CD4+) T-cell counts through Week 24

End point description:

Blood samples were collected and CD4+ cell count assessment by flow cytometry was carried out to evaluate the immunologic activity. Baseline is defined as the latest non-missing value prior to first dose of treatment according to date and time including unscheduled visits.
Analysis was performed on ITT-E Population that had data for CD4+ T-cells analysis as per timeline assessed.

End point type	Secondary

End point timeframe:

At Baseline (Day 1) and Week 24

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: cells per cubic millimeter (cells/mm^3)				
arithmetic mean (standard deviation)				
Baseline (Day 1) (N=22,20,22,21)	436.7 (± 161.93)	451.4 (± 164.86)	534.8 (± 200.99)	506.9 (± 165.14)
Week 24 (N=22,20,19,21)	753.4 (± 222.73)	661.0 (± 193.50)	756.1 (± 267.69)	627.5 (± 175.94)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ T-cell counts through Week 24

End point title	Change from Baseline in CD4+ T-cell counts through Week 24

End point description:

Blood samples were collected and CD4+ cell count assessment was carried out to evaluate the immunologic activity. Change from Baseline is defined as post-dose visit value minus Baseline value. Analysis was performed on ITT-E Population that had data for CD4+ T-cells analysis as per timeline assessed.

End point type	Secondary

End point timeframe:

At Week 24 compared to baseline (Day 1)

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	19	19	19
Units: cells/mm^3				
arithmetic mean (standard deviation)	317.7 (± 175.42)	200.6 (± 126.68)	241.2 (± 168.83)	139.5 (± 126.63)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with serious adverse events (SAEs) and deaths, up to end of continued access to treatment post-study termination (Day 478)

End point title	Number of participants with serious adverse events (SAEs) and deaths, up to end of continued access to treatment post-study termination (Day 478)

End point description:

An SAE is defined as any serious adverse event that, at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity and is a congenital anomaly/birth defect.
The study was terminated by the sponsor after primary analysis (at week 24). Adverse event data were collected up to end of continued access to treatment post-study termination (Day 478).
Analysis performed on Safety population, that included all randomized participants who took at least 1 dose 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 478)

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Participants				
SAEs	2	0	0	1
Death	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events (AEs) leading to discontinuation, up to end of continued access to treatment post-study termination (Day 478)

End point title	Number of participants with adverse events (AEs) leading to discontinuation, up to end of continued access to treatment post-study termination (Day 478)

End point description:

Number of participants who discontinued treatment due to AEs are presented.
The study was terminated by the sponsor after primary analysis (at week 24). Adverse event data were collected up to end of continued access to treatment post-study termination (Day 478).
Analysis performed on Safety population, that included all randomized participants who took at least 1 dose 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 478)

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Participants	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with adverse events of special interest (AESIs), up to end of continued access to treatment post-study termination (Day 478)

End point title	Number of participants with adverse events of special interest (AESIs), up to end of continued access to treatment post-study termination (Day 478)

End point description:

AEs of special interest (AESIs) included AEs related to QT prolongation, gastrointestinal (GI) intolerability/toxicity, psychiatric events, nervous system disorders, skin and subcutaneous tissue disorders and cardiac disorders.
The study was terminated by the sponsor after primary analysis (at week 24). Adverse event data were collected up to end of continued access to treatment post-study termination (Day 478).
Analysis performed on Safety population, that included all randomized participants who took at least 1 dose 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 478)

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Participants				
AEs related to QT prolongation	0	0	0	0
AEs related to GI intolerability/toxicity	5	7	8	5
AEs related to psychiatric events	0	3	0	4
AEs related to nervous system disorders	2	4	5	2
AEs related to skin, subcutaneous tissue disorder	4	0	4	0
AEs related to cardiac disorders	1	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who develop phenotypic resistance up to Week 24

End point title	Number of participants who develop phenotypic resistance up to Week 24

End point description:

Blood samples were collected for drug resistance testing to assess the development of viral resistance to GSK3640254 and other on-study Anti-Retroviral Therapy (ART) in participants experiencing virologic failure through Week 24. Only plasma HIV-1 RNA values determined by the central laboratory were used to assess virologic failure. PDVF was defined as having virologic non-response (HIV-1 RNA <1.0 log10 c/mL reduction from baseline and <200 copies/mL by Week 12, confirmed levels >=200 c/mL at or after Week 24 and plasma HIV-1 RNA <= 50 c/mL from testing on Week 24, virologic rebound (confirmed HIV-1 RNA >=200 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL).
Analysis was performed on ITT-E population.

End point type	Secondary

End point timeframe:

From Day 1 up to Week 24

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who develop genotypic resistance up to Week 24

End point title	Number of participants who develop genotypic resistance up to Week 24

End point description:

Blood samples were collected for drug resistance testing to assess the development of viral resistance to GSK3640254 through Week 24. New mutations were tabulated by drug class: integrase strand transfer inhibitor (INSTI), non-nucleoside reverse transcriptase inhibitor (NNRTI), nucleoside reverse transcriptase inhibitor (NRTI) and protease inhibitor (PI).
Protocol-Defined Virologic Failure (PDVF) was defined as having virologic non-response (HIV-1 RNA <1.0 log10 c/mL reduction from baseline and <200 copies/mL by Week 12, confirmed levels >=200 c/mL at or after Week 24 and plasma HIV-1 RNA <= 50 c/mL from testing on Week 24, virologic rebound (confirmed HIV-1 RNA >=200 copies/mL after confirmed consecutive HIV-1 RNA <50 copies/mL).
Analysis was performed on ITT-E population.

End point type	Secondary

End point timeframe:

From Day 1 up to Week 24

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	DTG 50 mg + Lamivudine (3TC) 300 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	20	22	21
Units: Participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Trough concentration (Ctrough) of GSK3640254 at Weeks 2, 4, 8, 12 and 24

End point title	Trough concentration (Ctrough) of GSK3640254 at Weeks 2, 4, 8, 12 and 24[2]

End point description:

Trough concentration (Ctrough) is the concentration reached by a drug immediately before the next dose is administered. This was determined to assess the steady-state exposure of GSK3640254 when given in combination with DTG.
Analysis performed on Pharmacokinetic population, which included all participants who received GSK3640254, underwent sparse PK sampling during the study, and provided evaluable GSK3640254 plasma concentration data, demographic and baseline characteristics, and/or information on concomitant medications. Only those participants with data available at specified time points were

analyzed for the specific category titles.

End point type	Secondary

End point timeframe:

At Weeks 2, 4, 8, 12 (PRE DOSE), 12 (2-6HR POST DOSE), 24 (PRE DOSE), 24 (2-6HR POST DOSE)

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: This endpoint presented the Ctrough analysis only for the arms that received one of the GSK3640254 doses (administered along with DTG), hence the DTG 50 mg + Lamivudine (3TC) 300 mg arm was not included in this endpoint.

End point values	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	22	20	22	
Units: nanogram per milliliter (ng/mL)				
geometric mean (confidence interval 95%)				
Week 2 (N=21,19,22)	340.2 (269.5 to 411.0)	549.9 (390.9 to 708.9)	724.2 (563.4 to 885.0)	
Week 4 (N=21,20,21)	417.8 (330.5 to 505.0)	632.7 (470.4 to 795.0)	799.6 (640.9 to 958.3)	
Week 8 (N=22,20,22)	386.2 (293.7 to 478.6)	646.6 (421.7 to 871.5)	821.1 (620.2 to 1022.0)	
Week 12 (PRE DOSE) (N=22,20,22)	481.3 (388.6 to 574.0)	611.4 (430.6 to 792.1)	877.2 (704.1 to 1050.3)	
Week 12 (2-6HR POST DOSE) (N=21,20,21)	767.8 (612.3 to 923.3)	1081.2 (759.5 to 1402.8)	1658.1 (1305.8 to 2010.4)	
Week 24 (PRE DOSE) (N=21,19,19)	396.0 (331.0 to 460.8)	570.1 (333.6 to 806.6)	848.8 (600.3 to 1097.4)	
Week 24 (2-6HR POST DOSE) (N=20,20,19)	759.0 (623.1 to 894.8)	1107.0 (660.8 to 1553.2)	1584.1 (1067.3 to 2100.9)	

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 up to end of continued access to treatment post-study termination (Day 478).

Adverse event reporting additional description:

The study was terminated by the sponsor after primary analysis (at week 24). As prespecified in Statistical analysis plan, AEs were collected up to end of continued access to treatment post-study termination (Day 478).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v26.0

Reporting groups

Reporting group title	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg

Reporting group description:

Participants with human immunodeficiency virus type 1 (HIV-1) orally received low dose (100 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Reporting group title	GSK3640254 150 mg + DTG 50 mg

Reporting group description:

Participants with HIV-1 orally received medium dose (150 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Reporting group title	GSK3640254 200 mg + DTG 50 mg

Reporting group description:

Participants with HIV-1 orally received high dose (200 mg) GSK3640254 tablet blinded and 50 mg DTG unblinded. Each participant received one tablet per day of each intervention up to Week 24.

Reporting group title	DTG 50 mg + Lamivudine (3TC) 300 mg

Reporting group description:

Participants with HIV-1 orally received unblinded 50 mg DTG one tablet and blinded 300 mg 3TC. Each participant received one capsule per day of each intervention up to Week 24.

Serious adverse events	GSK3640254 100 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 22 (9.09%)	0 / 20 (0.00%)	0 / 22 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	0 / 22 (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
General disorders and administration site conditions			

Non-cardiac chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anogenital dysplasia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	0 / 22 (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	DTG 50 mg + Lamivudine (3TC) 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 21 (4.76%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Guillain-Barre syndrome			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anogenital dysplasia			
subjects affected / exposed	1 / 21 (4.76%)		
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 mg + Dolutegravir (DTG) 50 mg	GSK3640254 150 mg + DTG 50 mg	GSK3640254 200 mg + DTG 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 22 (72.73%)	15 / 20 (75.00%)	17 / 22 (77.27%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Investigations			
Blood pressure increased			
subjects affected / exposed	2 / 22 (9.09%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Injury, poisoning and procedural complications			
Ligament sprain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	2 / 22 (9.09%)	3 / 20 (15.00%)	3 / 22 (13.64%)
occurrences (all)	2	4	3
Sciatica			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Dizziness			
subjects affected / exposed	0 / 22 (0.00%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	2 / 22 (9.09%)	2 / 20 (10.00%)	1 / 22 (4.55%)
occurrences (all)	2	2	1
Fatigue			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pyrexia			

subjects affected / exposed	1 / 22 (4.55%)	3 / 20 (15.00%)	0 / 22 (0.00%)
occurrences (all)	1	3	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 22 (0.00%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Haemorrhoids			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Faeces soft			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Dyspepsia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Diarrhoea			
subjects affected / exposed	1 / 22 (4.55%)	4 / 20 (20.00%)	5 / 22 (22.73%)
occurrences (all)	2	6	6
Abdominal pain upper			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Abdominal pain			
subjects affected / exposed	0 / 22 (0.00%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Abdominal discomfort			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	2 / 22 (9.09%)
occurrences (all)	0	0	2
Reproductive system and breast disorders			

Vascular disorders Hypertension			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Erectile dysfunction			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	2 / 22 (9.09%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	2	2	0
Catarrh			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Skin and subcutaneous tissue disorders			
Skin lesion			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	2 / 22 (9.09%)	0 / 20 (0.00%)	3 / 22 (13.64%)
occurrences (all)	2	0	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 22 (0.00%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Rotator cuff syndrome			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	1 / 22 (4.55%)	2 / 20 (10.00%)	0 / 22 (0.00%)
occurrences (all)	1	2	0
Arthralgia			

subjects affected / exposed	0 / 22 (0.00%)	2 / 20 (10.00%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Infections and infestations			
Folliculitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Urethritis chlamydial			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	3 / 22 (13.64%)	2 / 20 (10.00%)	5 / 22 (22.73%)
occurrences (all)	3	2	5
Herpes simplex			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Herpes zoster			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Monkeypox			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	3 / 22 (13.64%)
occurrences (all)	1	1	5
Oropharyngeal gonococcal infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Pharyngeal chlamydia infection			
subjects affected / exposed	1 / 22 (4.55%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Pharyngitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	1	2	2

Pharyngotonsillitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 20 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	2	2	0
Sinusitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 22 (9.09%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	2	1	2
Conjunctivitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	1 / 22 (4.55%)
occurrences (all)	0	2	1
Viral infection			
subjects affected / exposed	1 / 22 (4.55%)	1 / 20 (5.00%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Gastroeneteritis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 20 (5.00%)	2 / 22 (9.09%)
occurrences (all)	0	1	2

Non-serious adverse events	DTG 50 mg + Lamivudine (3TC) 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 21 (66.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Investigations			
Blood pressure increased			
subjects affected / exposed	0 / 21 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			

Ligament sprain subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Nervous system disorders Somnolence subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Sciatica subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0 2 / 21 (9.52%) 5 0 / 21 (0.00%) 0 1 / 21 (4.76%) 1		
General disorders and administration site conditions Influenza like illness subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 0 / 21 (0.00%) 0 0 / 21 (0.00%) 0		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Toothache subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 2 / 21 (9.52%) 2		

Haemorrhoids subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Faeces soft subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 2		
Diarrhoea subjects affected / exposed occurrences (all)	2 / 21 (9.52%) 2		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Abdominal pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Reproductive system and breast disorders Vascular disorders Hypertension subjects affected / exposed occurrences (all)	1 / 21 (4.76%) 1		
Erectile dysfunction subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Cough subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Catarrh			

subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Skin and subcutaneous tissue disorders Skin lesion subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 0 / 21 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1		
Musculoskeletal and connective tissue disorders Rotator cuff syndrome subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	 0 / 21 (0.00%) 0 1 / 21 (4.76%) 1 0 / 21 (0.00%) 0		
Infections and infestations Folliculitis subjects affected / exposed occurrences (all) Urethritis chlamydial subjects affected / exposed occurrences (all) COVID-19 subjects affected / exposed occurrences (all) Herpes simplex subjects affected / exposed occurrences (all)	 1 / 21 (4.76%) 1 1 / 21 (4.76%) 1 3 / 21 (14.29%) 3 0 / 21 (0.00%) 0		

Herpes zoster				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Influenza				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	3			
Monkeypox				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	3			
Oropharyngeal gonococcal infection				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Pharyngeal chlamydia infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Pharyngitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Pharyngotonsillitis				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Sinusitis				
subjects affected / exposed	0 / 21 (0.00%)			
occurrences (all)	0			
Upper respiratory tract infection				
subjects affected / exposed	3 / 21 (14.29%)			
occurrences (all)	6			
Conjunctivitis				
subjects affected / exposed	1 / 21 (4.76%)			
occurrences (all)	1			

Viral infection subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		
Gastroeneteritis subjects affected / exposed occurrences (all)	0 / 21 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 September 2022	The changes in this amendments were the reduction of the sample size of the participants and adjustment of number of participants among the 3 experimental arms.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported