Clinical trial results:
A Phase 3, Randomized, Clinical Study in HIV-1-Infected Heavily Treatment-Experienced Participants Evaluating the Antiretroviral Activity of Blinded Islatravir (ISL), Doravirine (DOR), and Doravirine/Islatravir (DOR/ISL), Each Compared to Placebo, and the Antiretroviral Activity, Safety, and Tolerability of Open-Label DOR/ISL

Summary

EudraCT number	2019-000588-26
Trial protocol	FR PT GB DE IT
Global end of trial date	01 November 2023

Results information

Result version number	v1 (current)
This version publication date	13 November 2024
First version publication date	13 November 2024

Trial information

Trial identification

Sponsor protocol code	8591A-019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04233216
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, Rahway, NJ, United States, P.O. Box 2000
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@merck.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	01 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2022
Global end of trial reached?	Yes
Global end of trial date	01 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a 2-part, phase 3 clinical study evaluating the antiretroviral activity and safety/tolerability of islatravir (ISL), doravirine (DOR), and a fixed dose combination (FDC) of DOR/ISL (also known as MK-8591A) in heavily treatment-experienced (HTE) participants with human immunodeficiency virus type 1 (HIV-1) infection. It is hypothesized that the percentage of participants receiving DOR/ISL to achieve ≥0.5 log10 decrease in HIV-1 ribonucleic acid (RNA) from study baseline (Day 1) to Day 8 is superior to placebo, each given in combination with failing antiretroviral therapy (ART).

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 March 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	Australia: 1
Country: Number of subjects enrolled	Canada: 1
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	South Africa: 6
Country: Number of subjects enrolled	Peru: 1
Country: Number of subjects enrolled	Russian Federation: 5
Country: Number of subjects enrolled	Ukraine: 1
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	35
EEA total number of subjects	8

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	34
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Heavily Treatment-Experienced (HTE) adult participants with Human Immunodeficiency Virus Type 1 (HIV-1) infection and currently on failing antiretroviral therapy (ART) were enrolled in this study.

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	ISL + ART

Arm description:

HTE participants with HIV-1 infection took islatravir (ISL) 0.75 mg once daily (QD) in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg doravirine (DOR)/0.75 mg ISL fixed dose combination (FDC) QD + optimized background therapy (OBT) from Day 8 to Week 97.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Islatravir
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg doravirine /0.75 mg islatravir FDC QD from day 8 to Day 97

Investigational medicinal product name	Islatravir
Investigational medicinal product code	
Other name	MK-8591
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

0.75 mg islatravir once daily (QD) from day 1 to 7

Arm title	DOR + ART

Arm description:

HTE participants with HIV-1 infection took DOR 100 mg QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.

Arm type	Experimental
Investigational medicinal product name	Doravirine
Investigational medicinal product code	
Other name	MK-1439
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg doravirine QD from day 1 to 7

Investigational medicinal product name	Doravirine/Islatravir
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg doravirine /0.75 mg islatravir fixed dose combination (FDC) QD from day 8 to Day 97

Arm title	DOR/ISL + ART

Arm description:

HTE participants with HIV-1 infection took 100 mg DOR/0.75 mg ISL FDC QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.

Arm type	Experimental
Investigational medicinal product name	Doravirine/Islatravir
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg doravirine /0.75 mg islatravir FDC QD from day 1 to Day 97

Arm title	Placebo + ART

Arm description:

HTE participants with HIV-1 infection took placebo QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.

Arm type	Placebo
Investigational medicinal product name	Placebo to islatravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to islatravir

Investigational medicinal product name	Doravirine/Islatravir
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg doravirine /0.75 mg islatravir FDC QD from day 8 to Day 97

Investigational medicinal product name	Placebo to doravirine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to doravirine

Number of subjects in period 1	ISL + ART	DOR + ART	DOR/ISL + ART
Started	7	14	7
Completed	6	9	4
Not completed	1	5	3
Physician decision	-	3	-
Consent withdrawn by subject	-	2	1
Lost to follow-up	1	-	2

Number of subjects in period 1	Placebo + ART
Started	7
Completed	5
Not completed	2
Physician decision	2
Consent withdrawn by subject	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	ISL + ART
Reporting group description:	
HTE participants with HIV-1 infection took islatravir (ISL) 0.75 mg once daily (QD) in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg doravirine (DOR)/0.75 mg ISL fixed dose combination (FDC) QD + optimized background therapy (OBT) from Day 8 to Week 97.	
Reporting group title	DOR + ART
Reporting group description:	
HTE participants with HIV-1 infection took DOR 100 mg QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	
Reporting group title	DOR/ISL + ART
Reporting group description:	
HTE participants with HIV-1 infection took 100 mg DOR/0.75 mg ISL FDC QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	
Reporting group title	Placebo + ART
Reporting group description:	
HTE participants with HIV-1 infection took placebo QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	

Reporting group values	ISL + ART	DOR + ART	DOR/ISL + ART
Number of subjects	7	14	7
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	14	6
From 65-84 years	0	0	1
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	46.6	48.6	54.0
standard deviation	± 12.7	± 11.8	± 10.0
Sex: Female, Male Units:			
Female	2	4	1
Male	5	10	6
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	5	5	0

White	2	7	6
More than one race	0	1	1
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	2	2
Not Hispanic or Latino	7	12	5
Unknown or Not Reported	0	0	0
Plasma HIV-1 RNA			
Units: Log10 copies/mL			
arithmetic mean	4.1	4.3	4.5
standard deviation	± 0.8	± 0.9	± 0.8
Custer of differentiation 4+ (CD4+) T-cell Count			
Units: cells/mm^3			
arithmetic mean	166.3	132.4	178.6
standard deviation	± 121.7	± 136.6	± 135.5

Reporting group values	Placebo + ART	Total	
Number of subjects	7	35	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	7	34	
From 65-84 years	0	1	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	44.6		
standard deviation	± 9.1	-	
Sex: Female, Male			
Units:			
Female	1	8	
Male	6	27	
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	2	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	11	
White	5	20	
More than one race	0	2	
Unknown or Not Reported	0	0	
Ethnicity (NIH/OMB)			
Units: Subjects			

Hispanic or Latino	0	4	
Not Hispanic or Latino	7	31	
Unknown or Not Reported	0	0	
Plasma HIV-1 RNA			
Units: Log10 copies/mL			
arithmetic mean	4.2		
standard deviation	± 0.7	-	
Custer of differentiation 4+ (CD4+) T-cell Count			
Units: cells/mm^3			
arithmetic mean	132.6		
standard deviation	± 100.7	-	

End points

End points reporting groups

Reporting group title	ISL + ART
Reporting group description:	
HTE participants with HIV-1 infection took islatravir (ISL) 0.75 mg once daily (QD) in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg doravirine (DOR)/0.75 mg ISL fixed dose combination (FDC) QD + optimized background therapy (OBT) from Day 8 to Week 97.	
Reporting group title	DOR + ART
Reporting group description:	
HTE participants with HIV-1 infection took DOR 100 mg QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	
Reporting group title	DOR/ISL + ART
Reporting group description:	
HTE participants with HIV-1 infection took 100 mg DOR/0.75 mg ISL FDC QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	
Reporting group title	Placebo + ART
Reporting group description:	
HTE participants with HIV-1 infection took placebo QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.	
Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol	
Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol	
Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol	
Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis
Subject analysis set description:	
HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol	
Subject analysis set title	Pooled Treatment

Subject analysis set type	Full analysis

Subject analysis set description:

HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol

Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis

Subject analysis set description:

HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol

Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis

Subject analysis set description:

HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol

Subject analysis set title	Pooled Treatment
Subject analysis set type	Full analysis

Subject analysis set description:

HTE participants with HIV-1 infection from the original four treatment groups (DOR, ISL, DOR/ISL FDC, placebo QD) treated in combination with failing ART from Day 1 to Day 7; followed by treatment with open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97 were pooled into a single group as planned per protocol

Primary: Percentage of participants receiving doravirine/islatravir (DOR/ISL) with ≥0.5 log10 change from Day 1 baseline to Day 8 in human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) compared to placebo treatment

End point title	Percentage of participants receiving doravirine/islatravir (DOR/ISL) with ≥0.5 log10 change from Day 1 baseline to Day 8 in human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) compared to placebo treatment[1]

End point description:

Participants with a ≥0.5 log10 decrease from Day 1 baseline to Day 8 in HIV-1 RNA were identified by the central laboratory with an Abbott Real Time Polymerase Chain Reaction (PCR) assay which has a lower limit of detection (LLOD) of 40 copies/mL The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Primary

End point timeframe:

Day 1 (baseline) and Day 8

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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[2]	0[3]	7	7
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)	85.7 (42.1 to 99.6)	0.0 (0.0 to 41.0)

Notes:

[2] - Only participants treated with DOR/ISL FDC or placebo were analyzed in this endpoint.

[3] - Only participants treated with DOR/ISL FDC or placebo were analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with ≥1 AEs through week 49

End point title	Percentage of participants with ≥1 AEs through week 49[4]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Primary

End point timeframe:

Up to 49 weeks

Notes:

[4] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	71.4	85.7	85.7	85.7

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants withdrawing from study treatment due to AE(s) through week 25

End point title	Percentage of participants withdrawing from study treatment due to AE(s) through week 25[5]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Primary

End point timeframe:

Up to 25 weeks

Notes:

[5] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	0.0	7.1	14.3	0.0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants withdrawing from study treatment due to AE(s) through week 49

End point title	Percentage of participants withdrawing from study treatment due to AE(s) through week 49[6]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Primary

End point timeframe:

Up to 49 weeks

Notes:

[6] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	0.0	14.3	14.3	0.0

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with ≥1 adverse events (AEs) through week 25

End point title	Percentage of participants with ≥1 adverse events (AEs) through week 25[7]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. The population

analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Primary

End point timeframe:

Up to 25 weeks

Notes:

[7] - 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: Statistical comparisons between treatment groups were neither planned nor performed for this primary endpoint.

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	42.9	85.7	85.7	85.7

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with ≥1 adverse events (AEs) through week 97

End point title	Percentage of participants with ≥1 adverse events (AEs) through week 97

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Secondary

End point timeframe:

Up to 97 weeks

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	85.7	100.0	85.7	100.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants discontinuing from study therapy due to AE(s) through week 97

End point title	Percentage of participants discontinuing from study therapy due to AE(s) through week 97

End point description:

An AE is any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

End point type	Secondary

End point timeframe:

Up to 97 weeks

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (not applicable)	0.0	21.4	28.6	14.3

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants receiving DOR or ISL (given with antiretroviral therapy [ART]) with ≥0.5 log10 change from Day 1 baseline to Day 8 HIV-1 RNA compared to placebo treatment

End point title	Percentage of participants receiving DOR or ISL (given with antiretroviral therapy [ART]) with ≥0.5 log10 change from Day 1 baseline to Day 8 HIV-1 RNA compared to placebo treatment

End point description:

Participants with a ≥0.5 log10 decrease from Day 1 baseline to Day 8 in HIV-1 RNA were identified by the central laboratory with an Abbott Real Time PCR assay which has a LLOD of 40 copies/mL Only participants treated with either DOR or ISL or placebo (given with ART) were analyzed in this outcome measure. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	0[8]	7
Units: Percentage of participants				
number (confidence interval 95%)	28.6 (3.7 to 71.0)	78.6 (49.2 to 95.3)	(to)	0.0 (0.0 to 41.0)

Notes:

[8] - Participants treated with DOR/ISL FDC were not analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 1 to Day 8 in HIV-1 RNA following treatment with DOR/ISL (given with ART), DOR, or ISL compared to placebo treatment

End point title	Mean change from baseline Day 1 to Day 8 in HIV-1 RNA following treatment with DOR/ISL (given with ART), DOR, or ISL compared to placebo treatment

End point description:

The change from baseline Day to Day 8 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-0.44 (-0.96 to 0.07)	-0.96 (-1.38 to -0.54)	-1.23 (-1.72 to -0.75)	0.03 (-0.15 to 0.21)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants receiving DOR/ISL (given with ART), DOR, or ISL with ≥1.0 log10 change from Day 1 baseline to Day 8 HIV-1 RNA compared to placebo treatment

End point title	Percentage of participants receiving DOR/ISL (given with ART), DOR, or ISL with ≥1.0 log10 change from Day 1 baseline to Day 8 HIV-1 RNA compared to placebo treatment

End point description:

Participants with a ≥1.0 log10 decrease from baseline (Day 1) to Day 8 in HIV-1 RNA were identified by at the central laboratory with an Abbott Real Time Polymerase Chain Reaction (PCR) assay which has a LLOD of 40 copies/mL The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (confidence interval 95%)	14.3 (0.4 to 57.9)	50.0 (23.0 to 77.0)	85.7 (42.1 to 99.6)	0.0 (0.0 to 41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants receiving DOR/ISL (given with ART) with ≥0.5 log10 change from Day 1 baseline to Day 8 in HIV-1 RNA compared to DOR or ISL treatment

End point title	Percentage of participants receiving DOR/ISL (given with ART) with ≥0.5 log10 change from Day 1 baseline to Day 8 in HIV-1 RNA compared to DOR or ISL treatment

End point description:

Participants with a ≥0.5 log10 decrease from baseline (Day 1) to Day 8 in HIV-1 RNA were identified by at the central laboratory with an Abbott Real Time PCR assay which has a lower limit of detection (LLOD) of 40 copies/mL Only participants treated with DOR/ISL or DOR alone or ISL alone were analyzed in this outcome measure. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	0[9]
Units: Percentage of participants				
number (confidence interval 95%)	28.6 (3.7 to 71.0)	78.6 (49.2 to 95.3)	85.7 (42.1 to 99.6)	(to)

Notes:

[9] - The group treated with placebo were not analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 1 to Day 8 in HIV-1 RNA following

treatment with DOR/ISL (given with ART) compared to DOR or ISL treatment	
End point title	Mean change from baseline Day 1 to Day 8 in HIV-1 RNA following treatment with DOR/ISL (given with ART) compared to DOR or ISL treatment

End point description:

The change from baseline Day 1 to Day 8in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the t-distribution. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	0[10]
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-0.44 (-0.96 to 0.07)	-0.96 (-1.38 to -0.54)	-1.23 (-1.72 to -0.75)	(to)

Notes:

[10] - The group treated with placebo were not analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 25 in HIV-1 RNA	
End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 25 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 1 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	85.3 (68.9 to 95.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants receiving DOR/ISL (given with ART) with ≥1.0 log10 change from Day 1 baseline to Day 8 in HIV-1 RNA compared to DOR or ISL treatment

End point title	Percentage of participants receiving DOR/ISL (given with ART) with ≥1.0 log10 change from Day 1 baseline to Day 8 in HIV-1 RNA compared to DOR or ISL treatment

End point description:

Participants receiving DOR/ISL with a ≥1.0 log10 decrease from baseline (Day 1) to Day 8 in HIV-1 RNA were identified by at the central laboratory with an Abbott Real Time PCR assay which has a lower limit of detection (LLOD) of 40 copies/mL Only participants treated with DOR/ISL or DOR alone or ISL alone were analyzed in this outcome measure. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	0[11]
Units: Percentage of participants				
number (confidence interval 95%)	14.3 (0.4 to 57.9)	50.0 (23.0 to 77.0)	85.7 (42.1 to 99.6)	(to)

Notes:

[11] - Participants treated with placebo were not analyzed in this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 97 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 97 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 1 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time

PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	84.6 (65.1 to 95.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 25 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 25 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 8 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	64.7 (46.5 to 80.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 49 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 49 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 8 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	67.7 (48.6 to 83.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 49 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 1 baseline to Week 49 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 1 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	80.6 (62.5 to 92.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 97 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥0.5 log10 change from Day 8 baseline to Week 97 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥0.5 log10 change from baseline Day 8 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	69.2 (48.2 to 85.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 8 baseline to Week 25 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group

	with ≥1.0 log10 change from Day 8 baseline to Week 25 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 8 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	58.8 (40.7 to 75.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 97 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 97 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 1 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	73.1 (52.2 to 88.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 49 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 49 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 1 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	71.0 (52.0 to 85.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 25 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 1 baseline to Week 25 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 1 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time

PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	67.6 (49.5 to 82.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 8 baseline to Week 97 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 8 baseline to Week 97 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 8 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	61.5 (40.6 to 79.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 8 baseline to Week 49 in HIV-1 RNA

End point title	Percentage of participants from the pooled treatment group with ≥1.0 log10 change from Day 8 baseline to Week 49 in HIV-1 RNA

End point description:

The percentage of participants in the pooled treatment group with ≥1.0 log10 change from baseline Day 8 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	61.3 (42.2 to 78.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <200 copies mL

End point title	Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <200 copies mL

End point description:

The percentage of participants with HIV-1 RNA <200 copies mL was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (confidence interval 95%)				
Day 1	0.0 (0.0 to 41.0)	0.0 (0.0 to 23.2)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)
Day 8	0.0 (0.0 to 41.0)	14.3 (1.8 to 42.8)	14.3 (0.4 to 57.9)	0.0 (0.0 to 41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 8 to Week 97 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 8 to Week 97 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-1.36 (-1.83 to -0.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 8 to Week 49 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 8 to Week 49 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-1.32 (-1.72 to -0.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 8 to Week 25 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 8 to Week 25 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-1.16 (-1.56 to -0.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 1 to Week 97 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 1 to Week 97 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 97 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-2.01 (-2.51 to -1.52)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 1 to Week 25 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 1 to Week 25 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 25 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-1.89 (-2.33 to -1.45)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean change from baseline Day 1 to Week 49 in HIV-1 RNA from the pooled treatment group

End point title	Mean change from baseline Day 1 to Week 49 in HIV-1 RNA from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 49 in HIV-1 RNA was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% confidence intervals (CIs) were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Log10 Copies/mL				
arithmetic mean (confidence interval 95%)	-2.00 (-2.47 to -1.53)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <50 copies mL

End point title	Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <50 copies mL

End point description:

The percentage of participants with HIV-1 RNA <50 copies mL was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (confidence interval 95%)				
Day 1	0.0 (0.0 to 41.0)	0.0 (0.0 to 23.2)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)
Day 8	0.0 (0.0 to 41.0)	14.3 (1.8 to 42.8)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 97

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 97

End point description:

The percentage of participants with HIV-1 RNA <200 copies mL at week 97 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	80.8 (60.6 to 93.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 49

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 49

End point description:

The percentage of participants with HIV-1 RNA <200 copies mL at week 49 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	77.4 (58.9 to 90.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 25

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <200 copies/mL at Week 25

End point description:

The percentage of participants with HIV-1 RNA <200 copies mL at week 25 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1

dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	64.7 (46.5 to 80.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <40 copies mL

End point title	Percentage of participants from Day 1 baseline to Day 8 with HIV-1 RNA <40 copies mL

End point description:

The percentage of participants with HIV-1 RNA <40 copies mL was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. The population analyzed was all randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized and had baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Day 8

End point values	ISL + ART	DOR + ART	DOR/ISL + ART	Placebo + ART
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	14	7	7
Units: Percentage of participants				
number (confidence interval 95%)				
Day 1	0.0 (0.0 to 41.0)	0.0 (0.0 to 23.2)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)
Day 8	0.0 (0.0 to 41.0)	14.3 (1.8 to 42.8)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 97

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 97

End point description:

The percentage of participants with HIV-1 RNA <40 copies mL at week 97 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	69.2 (48.2 to 85.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 49

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 49

End point description:

The percentage of participants with HIV-1 RNA <40 copies mL at week 49 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	71.0 (52.0 to 85.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 49

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 49

End point description:

The percentage of participants with HIV-1 RNA <50 copies mL at week 49 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	31			
Units: Percentage of participants				
number (confidence interval 95%)	71.0 (52.0 to 85.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 97

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 97

End point description:

The percentage of participants with HIV-1 RNA <50 copies mL at week 97 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1

dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	26			
Units: Percentage of participants				
number (confidence interval 95%)	69.2 (48.2 to 85.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 25

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <40 copies/mL at Week 25

End point description:

The percentage of participants with HIV-1 RNA <40 copies mL at week 25 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	58.8 (40.7 to 75.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 25

End point title	Percentage of participants from the pooled treatment group with HIV-1 RNA <50 copies/mL at Week 25

End point description:

The percentage of participants with HIV-1 RNA <50 copies mL at week 25 was determined by the central laboratory using an Abbott Real Time PCR assay with a LLOD of 40 copies/mL. The within-group 95% CIs were calculated based on the Clopper-Pearson method. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	34			
Units: Percentage of participants				
number (confidence interval 95%)	58.8 (40.7 to 75.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to OBT components at week 49

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to OBT components at week 49

End point description:

The prevalence of viral drug resistance to OBT components was based on the percentage of participants with TE RASs, which is calculated by dividing the number of participants with TE RASs by the number of participants tested for resistance, multiplied by 100. The RASs for OBT components were determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1 RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Percentage of participants				
number (not applicable)	28.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group with viral resistance-associated substitutions (RASs) at Week 25

End point title	Number of participants from the pooled treatment group with viral resistance-associated substitutions (RASs) at Week 25

End point description:

The number of participants from the pooled treatment group who had HIV-1 RNA ≥200 copies/mL with treatment emergent RAS at week 25 showing the type of RAS .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Participants				
RAS A98G	2			
RAS D67N	1			
RAS H221Y	1			
RAS K103S	1			
RAS K219E	1			
RAS L234I	1			
RAS M184V	1			
RAS M41L	1			
RAS N348I	1			
RAS V106A	3			
RAS V106I	2			
RAS V106M	1			
RAS V179I	2			
RAS Y318F	1			
RAS F53L	1			
RAS L90M	1			
RAS M36I	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to DOR at week 49

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to DOR at week 49

End point description:

The prevalence of viral drug resistance to DOR was based on the percentage of participants with TE RASs, which is calculated by dividing the number of participants with TE RASs by the number of participants tested for resistance, multiplied by 100. RASs for DOR were as follows: V106A/M, Y188C/L, F227C/H/I/L, M230I/L, L234I, Y318F, V108I, Y188F/H, G190E, H221Y, P236, and were determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1 RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Percentage of participants				
number (not applicable)	28.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to ISL at week 25

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to ISL at week 25

End point description:

The prevalence of viral drug resistance to ISL was based on the percentage of participants with TE RAS, which is calculated by dividing the number of participants with TE RAS by the number of participants tested for resistance, multiplied by 100. The RAS for ISL, M184V was determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1

RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Percentage of participants				
number (not applicable)	8.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to ISL at week 49

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to ISL at week 49

End point description:

The prevalence of viral drug resistance to ISL was based on the percentage of participants with TE RAS, which is calculated by dividing the number of participants with TE RAS by the number of participants tested for resistance, multiplied by 100. The RAS for ISL, M184V was determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1 RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Percentage of participants				
number (not applicable)	14.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to optimized background therapy (OBT) components at week 25

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to optimized background therapy (OBT) components at week 25

End point description:

The prevalence of viral drug resistance to OBT components was based on the percentage of participants with TE RASs, which is calculated by dividing the number of participants with TE RASs by the number of participants tested for resistance, multiplied by 100. The RASs for OBT components were determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1 RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Percentage of participants				
number (not applicable)	25.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to DOR at week 25

End point title	Percentage of participants from the pooled treatment group with treatment-emergent resistance-associated substitutions to DOR at week 25

End point description:

The prevalence of viral drug resistance to DOR was based on the percentage of participants with treatment-emergent (TE) resistance-associated substitutions (RASs), which is calculated by dividing the number of participants with TE RASs by the number of participants tested for resistance multiplied by 100. RASs for DOR were as follows: V106A/M, Y188C/L, F227C/H/I/L, M230I/L, L234I, Y318F, V108I, Y188F/H, G190E, H221Y, P236, and were determined by the central laboratory with the GenoSure Prime assay on post randomization samples from participants with HIV-1 RNA ≥200 copies/mL Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had HIV-1 RNA ≥200 copies/mL, and were tested for resistance.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: Percentage of participants				
number (not applicable)	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group with viral RASs at Week 49

End point title	Number of participants from the pooled treatment group with viral RASs at Week 49

End point description:

The number of participants from the pooled treatment group who had HIV-1 RNA ≥200 copies/mL with treatment emergent RAS at week 49 showing the type of RAS .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	7			
Units: Participants				
RAS A98G	1			
RAS D67N	1			
RAS K103S	1			
RAS K219E	1			
RAS M184V	1			
RAS M41L	1			
RAS N348I	1			
RAS V106A	2			
RAS V106I	1			
RAS V106M	1			
RAS V179I	2			
RAS F53L	1			
RAS L90M	1			
RAS M36I	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group with viral RASs at Week 97

End point title	Number of participants from the pooled treatment group with viral RASs at Week 97

End point description:

The number of participants from the pooled treatment group with treatment emergent RAS at week 97 are presented, showing the type of RAS .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	5			
Units: Participants				
RAS D67N	1			
RAS M41L	1			
RAS N348I	1			
RAS T215F	1			
RAS V106A	2			
RAS V106I	1			
RAS V106M	1			
RAS V179I	1			
RAS F53L	1			
RAS L90M	1			
RAS M36I	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 1 to Week 25 in cluster of differentiation 4+ (CD4+) T-cell counts from the pooled treatment group

End point title	Change from baseline Day 1 to Week 25 in cluster of differentiation 4+ (CD4+) T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 25 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations

include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	50.3 (27.8 to 72.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 25

End point title	Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 25

End point description:

The number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 25 is presented. .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: Participants	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 1 to Week 97 in CD4+ T-cell counts from the

pooled treatment group	
End point title	Change from baseline Day 1 to Week 97 in CD4+ T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 97 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	114.6 (54.7 to 174.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 1 to Week 49 in CD4+ T-cell counts from the pooled treatment group

End point title	Change from baseline Day 1 to Week 49 in CD4+ T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 1 to Week 49 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 1 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	86.9 (51.2 to 122.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 8 to Week 25 in CD4+ T-cell counts from the pooled treatment group

End point title	Change from baseline Day 8 to Week 25 in CD4+ T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 25 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 25

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	38.0 (9.6 to 66.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 97

End point title	Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 97

End point description:

The number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 97 is presented. .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: Participants	5			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 49

End point title	Number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 49

End point description:

The number of participants from the pooled treatment group exhibiting antiviral resistance of HIV-1 RNA ≥200 copies/mL at Week 49 is presented. .Analysis of the pooled treatment group was planned per protocol. The population analyzed was all randomized participants who received at least 1 dose of study intervention and had baseline data for those analyses that require baseline data. with confirmed HIV-1 RNA 200 copies/mL, and with available genotypic or phenotypic data that show evidence of resistance irrespective of viral load.

End point type	Secondary

End point timeframe:

Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: Participants	7			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 8 to Week 97 in CD4+ T-cell counts from the pooled treatment group

End point title	Change from baseline Day 8 to Week 97 in CD4+ T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 97 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 97

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	108.0 (47.9 to 168.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline Day 8 to Week 49 in CD4+ T-cell counts from the pooled treatment group

End point title	Change from baseline Day 8 to Week 49 in CD4+ T-cell counts from the pooled treatment group

End point description:

The change from baseline Day 8 to Week 49 in CD4+ T-cell counts was determined by the central laboratory.. The within-group 95% CIs were calculated based on the t-distribution. Analysis of the pooled treatment group was planned per protocol. The population analyzed was randomized participants who received at least 1 dose of study intervention, had baseline data for those analyses that require baseline data, and had not committed any major protocol violations. Examples of protocol violations include, but are not limited to nonadherence to study intervention; or becoming pregnant.

End point type	Secondary

End point timeframe:

Day 8 (baseline) and Week 49

End point values	Pooled Treatment			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	75.1 (36.9 to 113.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality (ACM): from randomization up to Week 49; Adverse Events (AE): from treatment (Day 1) Up to Week 97

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study intervention based on the treatment group to which they were randomized.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	ISL+ART

Reporting group description:

HTE participants with HIV-1 infection took islatravir (ISL) 0.75 mg once daily (QD) in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg doravirine (DOR)/0.75 mg ISL fixed dose combination (FDC) QD + optimized background therapy (OBT) from Day 8 to Week 97.

Reporting group title	Placebo+ART

Reporting group description:

HTE participants with HIV-1 infection took placebo QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.

Reporting group title	DOR/ISL+ART

Reporting group description:

HTE participants with HIV-1 infection took 100 mg DOR/0.75 mg ISL FDC QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97.

Reporting group title	DOR+ART

Reporting group description:

HTE participants with HIV-1 infection took DOR 100 mg QD in combination with failing ART from Day 1 to Day 7; followed by open-label 100 mg DOR/0.75 mg ISL FDC QD + OBT from Day 8 to Week 97

Serious adverse events	ISL+ART	Placebo+ART	DOR/ISL+ART
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 7 (28.57%)	2 / 7 (28.57%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Castleman's disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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			

Lower limb fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (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
Reactive gastropathy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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
COVID-19 pneumonia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (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
SARS-CoV-2 sepsis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (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
Postoperative wound infection			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (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	DOR+ART		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Castleman's disease			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reactive gastropathy			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis ulcerative			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
SARS-CoV-2 sepsis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	ISL+ART	Placebo+ART	DOR/ISL+ART
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	7 / 7 (100.00%)	6 / 7 (85.71%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Anogenital warts			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Kaposi's sarcoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Penile squamous cell carcinoma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nocturnal hypertension			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Intermittent claudication			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Exercise tolerance decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 7 (14.29%)	2 / 7 (28.57%)	1 / 7 (14.29%)
occurrences (all)	2	2	1
Feeling hot			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Injection site nodule			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dyspnoea exertional			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Increased viscosity of bronchial secretion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Suicidal ideation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Sleep terror			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Product issues			

Device dislocation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood calcium increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Blood glucose increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
CD4 lymphocytes decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Creatinine renal clearance decreased			
subjects affected / exposed	2 / 7 (28.57%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Fibrin D dimer increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Intestinal transit time increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Low density lipoprotein increased			

subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Neutrophil count decreased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Anaemia postoperative			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Accidental overdose			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Exposure to communicable disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Humerus fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Soft tissue injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			

subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Mitral valve incompetence			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Myelopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Motor dysfunction			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Head discomfort			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	1	0	1
Pancytopenia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			

Ear pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eye allergy			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Eye irritation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Retinal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Salivary hypersecretion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Haemorrhoids			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Diverticulum			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	2 / 7 (28.57%)
occurrences (all)	0	1	3
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Pityriasis rosea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1

Acanthosis nigricans			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Acute kidney injury			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Axillary mass			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Joint effusion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	2 / 7 (28.57%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Osteonecrosis			

subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Polyarthritis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	1 / 7 (14.29%)	2 / 7 (28.57%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Amoebiasis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Epididymitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Onychomycosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Oral candidiasis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Otitis externa			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Skin candida			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Respiratory tract infection viral			
subjects affected / exposed	1 / 7 (14.29%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	4	2	0
Fungal foot infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Increased appetite			

subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Obesity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DOR+ART		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Anogenital warts			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Kaposi's sarcoma			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Penile squamous cell carcinoma			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Nocturnal hypertension			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Intermittent claudication			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Hypertension			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Exercise tolerance decreased			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Feeling hot			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Injection site nodule			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Dyspnoea exertional			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Increased viscosity of bronchial secretion			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Suicidal ideation			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Sleep terror			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Depressed mood			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Product issues			
Device dislocation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Blood calcium increased			

subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Blood cholesterol increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Blood creatine phosphokinase increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Blood glucose increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
C-reactive protein increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
CD4 lymphocytes decreased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Creatinine renal clearance decreased				
subjects affected / exposed	3 / 14 (21.43%)			
occurrences (all)	3			
Fibrin D dimer increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Intestinal transit time increased				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Low density lipoprotein increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Lymphocyte count decreased				
subjects affected / exposed	5 / 14 (35.71%)			
occurrences (all)	6			
Weight increased				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			

Weight decreased subjects affected / exposed occurrences (all) Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0 0 / 14 (0.00%) 0		
Injury, poisoning and procedural complications Anaemia postoperative subjects affected / exposed occurrences (all) Accidental overdose subjects affected / exposed occurrences (all) Exposure to communicable disease subjects affected / exposed occurrences (all) Humerus fracture subjects affected / exposed occurrences (all) Skin laceration subjects affected / exposed occurrences (all) Soft tissue injury subjects affected / exposed occurrences (all) Tendon rupture subjects affected / exposed occurrences (all) Wrist fracture subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1 2 / 14 (14.29%) 2 1 / 14 (7.14%) 1 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0		
Cardiac disorders Mitral valve incompetence subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1		
Nervous system disorders			

Somnolence			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Myelopathy			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Motor dysfunction			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	3		
Head discomfort			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Pancytopenia			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Cataract			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Eye allergy			

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Eye irritation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Retinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Dental caries			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Abdominal pain lower			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Anal rash			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Salivary hypersecretion			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		

Dyspepsia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Diverticulum			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	4 / 14 (28.57%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Pityriasis rosea			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Night sweats			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Acanthosis nigricans			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Dysuria			

subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Acute kidney injury			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Axillary mass			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Joint effusion			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Muscle tightness			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Osteonecrosis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Polyarthritis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Cellulitis			

subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
COVID-19				
subjects affected / exposed	4 / 14 (28.57%)			
occurrences (all)	4			
Bronchitis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Amoebiasis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Epididymitis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Fungal skin infection				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Onychomycosis				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Oral candidiasis				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Oral herpes				
subjects affected / exposed	0 / 14 (0.00%)			
occurrences (all)	0			
Otitis externa				
subjects affected / exposed	1 / 14 (7.14%)			
occurrences (all)	1			
Respiratory tract infection				

subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	2		
Upper respiratory tract infection			
subjects affected / exposed	2 / 14 (14.29%)		
occurrences (all)	2		
Skin candida			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Respiratory tract infection viral			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	3		
Fungal foot infection			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Increased appetite			
subjects affected / exposed	0 / 14 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		
Obesity			
subjects affected / exposed	1 / 14 (7.14%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2020	Amendment 01: Assessment of fasting lipid and glucose profiles were added to the protocol.
24 June 2020	Amendment 02: Allow participants to rescreen following consultation with the Sponsor. The lower age limit of 12 years was removed.
08 January 2021	Amendment 03: Extend Part 2 of the study from 48 weeks to 96 weeks of open-label intervention with DOR/ISL + OBT, permit continued administration of study intervention in participants who become pregnant, add a discontinuation criterion if a participant chooses to breastfeed, and add a Per-Protocol analysis to the SAP.
12 July 2021	Amendment 06: Modified inclusion criteria to clearly characterize the HTE study population as individuals with no more than 2 fully active antiretroviral drugs across all approved antiretroviral classes.
23 February 2022	Amendment 08: Given the findings of decreases in CD4+ T-cell and total lymphocyte counts in clinical studies evaluating ISL, the protocol is being amended to increase the frequency of monitoring of CD4+ T-cell and total lymphocyte counts and to specify the management of participants who meet protocol-defined decreases in CD4+ T-cell and/or total lymphocyte counts.
26 September 2022	Amendment 09: Merck Sharp & Dohme Corp. underwent an entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA. This conversion resulted only in an entity name change and update to the address.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported