Clinical trial results:
A Phase 2B, Randomized, Double-Blind, Active-Comparator-Controlled, Dose-Ranging Clinical Trial to Evaluate the Safety, Tolerability, Antiretroviral Activity, and Pharmacokinetics of MK-8591 Given in Combination with Doravirine (DOR) and Lamivudine (3TC) in HIV-1-Infected Treatment-Naïve Adults

Summary

EudraCT number	2017-000437-32
Trial protocol	GB FR
Global end of trial date	09 March 2022

Results information

Result version number	v1 (current)
This version publication date	17 March 2023
First version publication date	17 March 2023

Trial information

Trial identification

Sponsor protocol code	MK-8591-011

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03272347
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme LLC
Sponsor organisation address	126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065
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	09 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2021
Global end of trial reached?	Yes
Global end of trial date	09 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the safety, tolerability, antiretroviral activity, and pharmacokinetics of 3 doses of islatravir (MK-8591) in combination with doravirine (DOR) and lamivudine (3TC) administered to antiretroviral treatment-naïve adult participants with human immunodeficiency virus type 1 (HIV-1) infection.

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	27 November 2017
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	Chile: 40
Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	United States: 51
Worldwide total number of subjects	123
EEA total number of subjects	24

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)	121
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Treatment-naïve participants ≥18 years of age with human immunodeficiency virus type 1 (HIV-1) were enrolled in this study.

Pre-assignment

Screening details:

A total of 197 participants were screened and 123 were randomized in the study. All non-randomized participants were screen failures.

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	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Islatravir 0.25 mg

Arm description:

In Part 1, participants were treated once daily (QD) with 0.25 mg islatravir, 100 mg doravirine (DOR), 300 mg lamivudine (3TC), and placebo to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no Protocol-defined Virologic Failure (PDVF) discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

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:

Doravirine 100 mg is orally administered QD in tablet form for up to 144 weeks

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:

Islatravir at 0.25 mg was orally administered QD in capsule form for up to 52 weeks. After Week 60 a selected open label dose may be administered.

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:

Fixed dose combination of islatravir 0.75 mg/doravirine 100 mg orally administered QD in tablet form for 48 weeks

Investigational medicinal product name	Placebo to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to doravirine/lamivudine/tenofovir disoproxil fumarate is orally administered QD in tablet form for up to 52 weeks

Investigational medicinal product name	Lamivudine
Investigational medicinal product code	
Other name	3TC
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lamivudine 300 mg is orally administered QD in tablet form for up to 52 weeks

Arm title	Islatravir 0.75 mg

Arm description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Arm type	Experimental
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:

Islatravir at 0.75 mg was orally administered QD in capsule form for up to 52 weeks. After Week 60 a selected open label dose may be administered.

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:

Doravirine 100 mg is orally administered QD in tablet form for up to 144 weeks

Investigational medicinal product name	Lamivudine
Investigational medicinal product code	
Other name	3TC
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lamivudine 300 mg is orally administered QD in tablet form for up to 52 weeks

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:

Fixed dose combination of islatravir 0.75 mg/doravirine 100 mg orally administered QD in tablet form for 48 weeks

Investigational medicinal product name	Placebo to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to doravirine/lamivudine/tenofovir disoproxil fumarate is orally administered QD in tablet form for up to 52 weeks

Arm title	Islatravir 2.25 mg

Arm description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Arm type	Experimental
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:

Islatravir at 2.25 mg was orally administered QD in capsule form for up to 52 weeks. After Week 60 a selected open label dose may be administered.

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:

Doravirine 100 mg is orally administered QD in tablet form for up to 144 weeks

Investigational medicinal product name	Lamivudine
Investigational medicinal product code	
Other name	3TC
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Lamivudine 300 mg is orally administered QD in tablet form for up to 52 weeks

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:

Fixed dose combination of islatravir 0.75 mg/doravirine 100 mg orally administered QD in tablet form for 48 weeks

Investigational medicinal product name	Placebo to Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo to doravirine/lamivudine/tenofovir disoproxil fumarate is orally administered QD in tablet form for up to 52 weeks

Arm title	DOR/3TC/TDF

Arm description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Arm type	Active comparator
Investigational medicinal product name	Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate
Investigational medicinal product code	
Other name	MK-1439A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Fixed dose combination of 100 mg doravirine + 300 mg lamivudine + 300 mg tenofovir disoproxil fumarate is orally administered QD in tablet form for up to 144 weeks.

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 to islatravir is orally administered QD in capsule form for up to 52 weeks

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:

Fixed dose combination of islatravir 0.75 mg/doravirine 100 mg orally administered QD in tablet form for 48 weeks

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

Dosage and administration details:

Placebo to Lamivudine is orally administered QD in tablet form for up to 52 weeks

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 to Doravirine is orally administered QD in tablet form for up to 52 weeks

Number of subjects in period 1	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg
Started	31	30	31
Treated	29	30	31
Completed	20	24	19
Not completed	11	6	12
Adverse event, serious fatal	-	-	-
Physician decision	4	2	5
Consent withdrawn by subject	5	1	2
Screen Failure	1	-	-
Lost to follow-up	1	3	5

Number of subjects in period 1	DOR/3TC/TDF
Started	31
Treated	31
Completed	24
Not completed	7
Adverse event, serious fatal	1
Physician decision	4
Consent withdrawn by subject	1
Screen Failure	-
Lost to follow-up	1

Baseline characteristics

Reporting groups	
Reporting group title	Islatravir 0.25 mg

Reporting group description:

In Part 1, participants were treated once daily (QD) with 0.25 mg islatravir, 100 mg doravirine (DOR), 300 mg lamivudine (3TC), and placebo to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no Protocol-defined Virologic Failure (PDVF) discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	Islatravir 0.75 mg

Reporting group description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	Islatravir 2.25 mg

Reporting group description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	DOR/3TC/TDF

Reporting group description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg
Number of subjects	31	30	31
Age categorical Units: Participants			
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)	30	30	30
From 65-84 years	1	0	1
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	32.3	30.0	32.4
standard deviation	± 13.3	± 9.0	± 11.8
Sex: Female, Male			
Units: Participants			
Female	1	3	3
Male	30	27	28
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	6	6	8
White	24	24	21
More than one race	0	0	2
Unknown or Not Reported	1	0	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	14	19	12
Not Hispanic or Latino	16	11	18
Unknown or Not Reported	1	0	1
HIV-1 RNA Levels at Screening			
Randomization was stratified by the screening HIV-1 RNA levels (<=100,000 copies/mL or >100,000 copies/mL).			
Units: Subjects			
<=100,000 copies/mL	24	23	23
>100,000 copies/mL	7	7	8
CD4+ T-Cell Count			
Two untreated participants from the Islatravir 0.25 mg treatment group were not analyzed.			
Units: cells/mm^3			
arithmetic mean	450.8	538.5	469.6
standard deviation	± 170.0	± 165.5	± 203.3

Reporting group values	DOR/3TC/TDF	Total	
Number of subjects	31	123	
Age categorical			
Units: Participants			
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)	31	121	
From 65-84 years	0	2	

85 years and over	0	0	

Age Continuous Units: Years			
arithmetic mean	29.4		
standard deviation	± 8.9	-	
Sex: Female, Male Units: Participants			
Female	3	10	
Male	28	113	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	1	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	5	25	
White	24	93	
More than one race	0	2	
Unknown or Not Reported	1	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	15	60	
Not Hispanic or Latino	15	60	
Unknown or Not Reported	1	3	
HIV-1 RNA Levels at Screening			
Randomization was stratified by the screening HIV-1 RNA levels (<=100,000 copies/mL or >100,000 copies/mL).			
Units: Subjects			
<=100,000 copies/mL	24	94	
>100,000 copies/mL	7	29	
CD4+ T-Cell Count			
Two untreated participants from the Islatravir 0.25 mg treatment group were not analyzed.			
Units: cells/mm^3			
arithmetic mean	508.5		
standard deviation	± 206.8	-	

End points

End points reporting groups

Reporting group title	Islatravir 0.25 mg

Reporting group description:

In Part 1, participants were treated once daily (QD) with 0.25 mg islatravir, 100 mg doravirine (DOR), 300 mg lamivudine (3TC), and placebo to doravirine/lamivudine/tenofovir disoproxil fumarate (DOR/3TC/TDF) for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no Protocol-defined Virologic Failure (PDVF) discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	Islatravir 0.75 mg

Reporting group description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	Islatravir 2.25 mg

Reporting group description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Reporting group title	DOR/3TC/TDF

Reporting group description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	DOR/ISL Continued (Part 4)
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 4, beginning with week 144, participants who received the fixed dose combination of doravirine (100mg)/islatravir (0.75mg) QD open label in Part 3 and continued treatment through Week 192.

Subject analysis set title	DOR/ISL Switch (Part 4)
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 4, beginning with week 144, participants who received DOR/3TC/TDF QD open label up to Week 144 were switched to the fixed dose combination of doravirine (100mg)/islatravir (0.75mg) QD open label and continued treatment until Week 192

Subject analysis set title	DOR/ISL Continued (Part 4)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 4, beginning with week 144, participants who received the fixed dose combination of doravirine (100mg)/islatravir (0.75mg) QD open label in Part 3 and continued treatment through Week 192.

Subject analysis set title	DOR/ISL Switch (Part 4)
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 4, beginning with week 144, participants who received DOR/3TC/TDF QD open label up to Week 144 were switched to the fixed dose combination of doravirine (100mg)/islatravir (0.75mg) QD open label and continued treatment until Week 192

Subject analysis set title	Islatravir 0.25 mg
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	Islatravir 0.75 mg
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	Islatravir 2.25 mg
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	DOR/3TC/TDF
Subject analysis set type	Full analysis

Subject analysis set description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	Islatravir 0.25 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all

participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	Islatravir 0.75 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	Islatravir 2.25 mg
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Subject analysis set title	DOR/3TC/TDF
Subject analysis set type	Safety analysis

Subject analysis set description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144. In Part 4, beginning with Week 144, participants received the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Primary: Percentage of participants with HIV-1 RNA <50 copies/mL at Week 24

End point title	Percentage of participants with HIV-1 RNA <50 copies/mL at Week 24

End point description:

Blood samples were collected and plasma human immunodeficiency virus 1 (HIV-1) ribonucleic acid (RNA) were quantified using a real time polymerase chain reaction (PCR) assay with a lower limit of detection of 40 copies/mL. Missing values were counted as failure. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Primary

End point timeframe:

Week 24

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	29	30	31	31
Units: Percentage of participants				
number (not applicable)	93.1	100.0	90.3	90.3

Statistical analyses

Statistical analysis title	Treatment difference in percent response
Statistical analysis description:	
The 95% confidence intervals (CIs) were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).	
Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.5
upper limit	18.3

Statistical analysis title	Treatment difference in percent response
Statistical analysis description:	
The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16
upper limit	16.3

Statistical analysis title	Treatment difference in percent response
Statistical analysis description:	
The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference	

weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	9.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.8
upper limit	23

Primary: Percentage of participants with HIV-1 RNA <50 copies/mL at Week 48

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

End point description:

Blood samples were collected and plasma HIV-1 RNA were quantified using a real time PCR assay with a lower limit of detection of 40 copies/mL. Missing values were counted as failure. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Primary

End point timeframe:

Week 48

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: Percentage of participants				
number (not applicable)	89.7	90.0	77.4	83.9

Statistical analyses

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	24.4

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-6.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.1
upper limit	14.8

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	24.6

Primary: Number of participants experiencing adverse events (AEs) up to Week 144	
End point title	Number of participants experiencing adverse events (AEs) up to Week 144

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. All randomized participants who received at least 1 dose of study treatment, corresponding to the study treatment they actually received.

End point type	Primary

End point timeframe:

Up to 144 weeks

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: Participants	26	27	24	27

Statistical analyses

Statistical analysis title	Difference in % Islatravir vs Active Comparator

Statistical analysis description:

Based on Miettinen & Nurminen method.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	2.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.7
upper limit	20.5

Statistical analysis title	Difference in % Islatravir vs Active Comparator

Statistical analysis description:

Based on Miettinen & Nurminen method.

Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	-9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.4
upper limit	10.1

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description:	
Based on Miettinen & Nurminen method.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	20.8

Primary: Number of participants discontinuing study drug due to AEs up to Week 144

End point title	Number of participants discontinuing study drug due to AEs up to Week 144

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. All randomized participants who received at least 1 dose of study treatment, corresponding to the study treatment they actually received.

End point type	Primary

End point timeframe:

Up to 144 weeks

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: Participants	1	0	2	1

Statistical analyses

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description: Based on Miettinen & Nurminen method	
Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	14.5

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description: Based on Miettinen & Nurminen method	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in %
Point estimate	-3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.4
upper limit	8.5

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description: Based on Miettinen & Nurminen method	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	3.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.8
upper limit	18.1

Secondary: Percentage of participants with HIV-1 RNA <50 copies/mL up to 24 weeks after 3TC and placebo are discontinued from the regimen

End point title	Percentage of participants with HIV-1 RNA <50 copies/mL up to 24 weeks after 3TC and placebo are discontinued from the regimen

End point description:

Blood samples were collected and plasma HIV-1 RNA were quantified using a real time PCR assay with a lower limit of detection of 40 copies/mL, and missing values were counted as failure. 3TC and placebo are discontinued from the regimen from Week 24 up to Week 52. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Up to 24 weeks after 3TC and Placebo are discontinued from the regimen (up to approximately 60 weeks after initiating treatment)

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	27	28
Units: Percentage of participants				
number (not applicable)	86.2	90.0	88.9	96.4

Statistical analyses

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-9.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26.1
upper limit	6.6

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-7.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	8.8

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-6.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.5
upper limit	9.1

Secondary: Percentage of participants with HIV-1 RNA <50 copies/mL up to 48 weeks after 3TC and placebo are discontinued from the regimen

End point title	Percentage of participants with HIV-1 RNA <50 copies/mL up to 48 weeks after 3TC and placebo are discontinued from the regimen

End point description:

Blood samples were collected and plasma HIV-1 RNA were quantified using a real time PCR assay with a lower limit of detection of 40 copies/mL, and missing values were counted as failure. 3TC and placebo are discontinued from the regimen from Week 24 up to Week 52. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Up to 48 weeks

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	27	28
Units: Percentage of participants				
number (not applicable)	62.1	56.7	59.3	60.7

Statistical analyses

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.4
upper limit	27.7

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF

Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-3.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.6
upper limit	22.1

Statistical analysis title	Treatment difference in percent response

Statistical analysis description:

The 95% CIs were calculated using stratum-adjusted Mantel-Haenszel method with the difference weighted by the harmonic mean of sample size per arm for each stratum (screening HIV-1 RNA ≤100,000 or >100,000 copies/mL).

Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.7
upper limit	25.2

Secondary: Percentage of participants with HIV-1 RNA <50 copies/mL up to 48 weeks after starting open-label doravirine/islatravir regimen (Part 4)

End point title	Percentage of participants with HIV-1 RNA <50 copies/mL up to 48 weeks after starting open-label doravirine/islatravir regimen (Part 4)

End point description:

Blood samples were collected and plasma HIV-1 RNA were quantified using a real time PCR assay with a lower limit of detection of 40 copies/mL. Missing values were counted as failure. The percentage of participants with HIV-1 RNA <50 copies in Part 4 are reported. Per protocol, all randomized participants who entered Part 4 and either continued treatment with DOR/ISL from Part 3 or switched from DOR/3TC/TDF in Part 3 to DOR/ISL in Part 4; and received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data were analyzed.

End point type	Secondary

End point timeframe:

Up to Week 192

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	22		
Units: Percentage of participants				
number (not applicable)	85.1	95.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in mature T-helper (CD4+ T)-cell count at Week 24

End point title	Change from baseline in mature T-helper (CD4+ T)-cell count at Week 24

End point description:

Blood samples were collected and cluster of differentiation (CD4)+ T-cell counts were performed, where baseline measurements are defined as the Day 1 value, and baseline values were carried forward for participants who discontinue due to lack of efficacy. Post-baseline data were collected after the first dose of study medication through 14 days after the last dose of study medication. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	220.5 (170.3 to 270.8)	192.8 (117.9 to 267.7)	142.9 (89.9 to 196.0)	142.1 (105.7 to 178.5)

Statistical analyses

Statistical analysis title	Treatment difference in T-cell count

Statistical analysis description:

The 95% CI for mean difference in CD4 change was based on t-distribution.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	78.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	18.8
upper limit	138.1

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63
upper limit	64.7

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	50.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.7
upper limit	133.1

Secondary: Change from baseline in CD4+ T-cell count at Week 48	
End point title	Change from baseline in CD4+ T-cell count at Week 48

End point description:

Blood samples were collected and CD4+ T-cell counts were performed, where baseline measurements are defined as the Day 1 value, and baseline values were carried forward for participants who discontinue due to lack of efficacy. Post-baseline data were collected after the first dose of study medication through 14 days after the last dose of study medication. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	182.0 (119.6 to 244.5)	183.0 (124.7 to 241.2)	100.7 (25.0 to 176.3)	181.4 (137.2 to 225.6)

Statistical analyses

Statistical analysis title	Treatment difference in T-cell count

Statistical analysis description:

The 95% CI for mean difference in CD4 change was based on t-distribution.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-74.1
upper limit	75.3

Statistical analysis title	Treatment difference in T-cell count

Statistical analysis description:

The 95% CI for mean difference in CD4 change was based on t-distribution.

Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-70.7
upper limit	73.8

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-80.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-165.6
upper limit	4

Secondary: Change from baseline in CD4+ T-cell count at Week 96

End point title	Change from baseline in CD4+ T-cell count at Week 96

End point description:

Blood samples were collected and CD4+ T-cell counts were performed, where baseline measurements are defined as the Day 1 value, and baseline values were carried forward for participants who discontinue due to lack of efficacy. Post-baseline data were collected after the first dose of study medication through 14 days after the last dose of study medication. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Baseline and Week 96

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	243.4 (165.5 to 321.3)	161.3 (90.2 to 232.4)	136.5 (57.0 to 216.0)	268.9 (188.5 to 349.3)

Statistical analyses

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description: The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-25.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-134.8
upper limit	83.8

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description: The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-132.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-242.9
upper limit	-21.9

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description: The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF

Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-107.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-212.1
upper limit	-3.1

Secondary: Change from baseline in CD4+ T-cell count at Week 144

End point title	Change from baseline in CD4+ T-cell count at Week 144

End point description:

Blood samples were collected and CD4+ T-cell counts were performed, where baseline measurements are defined as the Day 1 value, and baseline values were carried forward for participants who discontinue due to lack of efficacy. Post-baseline data were collected after the first dose of study medication through 14 days after the last dose of study medication. All randomized participants who received at least 1 dose of study treatment and have baseline data for those analyses that require baseline data.

End point type	Secondary

End point timeframe:

Baseline and Week 144

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	204.4 (102.0 to 306.7)	209.0 (111.5 to 306.6)	162.9 (70.2 to 255.5)	270.0 (183.2 to 356.8)

Statistical analyses

Statistical analysis title	Treatment difference in T-cell count

Statistical analysis description:

The 95% CI for mean difference in CD4 change was based on t-distribution.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-65.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-195.3
upper limit	64

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-107.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-231.2
upper limit	16.9

Statistical analysis title	Treatment difference in T-cell count
Statistical analysis description:	
The 95% CI for mean difference in CD4 change was based on t-distribution.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	61
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Treatment Difference
Point estimate	-61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-188.7
upper limit	66.8

Secondary: Change from baseline in CD4+ T-cell count at Week 192 (Part 4)

End point title	Change from baseline in CD4+ T-cell count at Week 192 (Part 4)

End point description:

Blood samples were collected and CD4+ T-cell counts were performed, where baseline measurements are defined as the Week 144 value. The change from baseline in CD4+ T-cell count at Week 192 (Part 4) are reported. Per protocol, all randomized participants who entered Part 4 and either continued treatment with DOR/ISL from Part 3 or switched from DOR/3TC/TDF in Part 3 to DOR/ISL in Part 4; and received at least 1 dose of study treatment and have baseline data for those analyses that require

baseline data were analyzed.

End point type	Secondary

End point timeframe:

Baseline and Week 192

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	21		
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	3.8 (-1.9 to 9.5)	-3.4 (-12.0 to 5.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants experiencing AEs through 24 weeks after 3TC and placebo are discontinued from the regimen

End point title	Number of participants experiencing AEs through 24 weeks after 3TC and placebo are discontinued from the regimen

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. 3TC and placebo are discontinued from the regimen from Week 24 up to Week 52. All randomized participants who received at least 1 dose of study treatment, corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	27	28
Units: Participants	18	20	14	16

Statistical analyses

Statistical analysis title	Difference in % Islatravir vs Active Comparator

Statistical analysis description:

Based on Miettinen & Nurminen method.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	4.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.3
upper limit	29.6

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description: Based on Miettinen & Nurminen method.	
Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	-5.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.6
upper limit	20.7

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description: Based on Miettinen & Nurminen method.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.4
upper limit	33.5

Secondary: Number of participants discontinuing study drug due to AEs through 24 weeks after 3TC and placebo are discontinued from the regimen

End point title	Number of participants discontinuing study drug due to AEs through 24 weeks after 3TC and placebo are discontinued from the regimen

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. 3TC and placebo are discontinued from the regimen from Week 24 up to Week 52. All randomized participants who received at least 1 dose of study treatment, corresponding to the study treatment they actually received.

End point type	Secondary

End point timeframe:

Up to 24 weeks

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	27	28
Units: Participants	0	0	2	1

Statistical analyses

Statistical analysis title	Difference in % Islatravir vs Active Comparator

Statistical analysis description:

Based on Miettinen & Nurminen method.

Comparison groups	Islatravir 0.25 mg v DOR/3TC/TDF
Number of subjects included in analysis	57
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	8.5

Statistical analysis title	Difference in % Islatravir vs Active Comparator

Statistical analysis description:

Based on Miettinen & Nurminen method.

Comparison groups	Islatravir 2.25 mg v DOR/3TC/TDF

Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	3.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.5
upper limit	20.6

Statistical analysis title	Difference in % Islatravir vs Active Comparator
Statistical analysis description:	
Based on Miettinen & Nurminen method.	
Comparison groups	Islatravir 0.75 mg v DOR/3TC/TDF
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Difference in %
Point estimate	-3.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.9
upper limit	8.2

Secondary: Number of participants experiencing AEs from Week 96 through study duration

End point title	Number of participants experiencing AEs from Week 96 through study duration
End point description:	
An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. Per protocol, all randomized participants who received at least 1 dose of open label study treatment in Part 3 or Part 4, corresponding to the study treatment they actually received were analyzed.	
End point type	Secondary
End point timeframe:	
Week 96 up to Week 192	

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: Participants	12	19	11	12

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	22		
Units: Participants	36	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants discontinuing study drug due to AEs from Week 96 through study duration

End point title	Number of participants discontinuing study drug due to AEs from Week 96 through study duration

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. Per protocol, all randomized participants who received at least 1 dose of open label study treatment in Part 3 or Part 4, corresponding to the study treatment they actually received were analyzed.

End point type	Secondary

End point timeframe:

Week 96 up to Week 192

End point values	Islatravir 0.25 mg	Islatravir 0.75 mg	Islatravir 2.25 mg	DOR/3TC/TDF
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	29	30	31	31
Units: Participants	1	0	0	0

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	22		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants experiencing AEs during open label doravirine/islatravir treatment after week 144 up to week 192 (Part 4)

End point title	Number of participants experiencing AEs during open label doravirine/islatravir treatment after week 144 up to week 192 (Part 4)

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. The number of participants who experienced AEs during Part 4 are reported. Per protocol, all randomized participants who entered Part 4 and either continued treatment with DOR/ISL from Part 3 or switched from DOR/3TC/TDF in Part 3 to DOR/ISL in Part 4; and received at least 1 dose of study treatment, corresponding to the study treatment they actually received were analyzed.

End point type	Secondary

End point timeframe:

Week 144 up to Week 192

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	22		
Units: Participants	36	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants discontinuing study drug due to AEs during open label doravirine/islatravir treatment after week 144 up to week 192 (Part 4)

End point title	Number of participants discontinuing study drug due to AEs during open label doravirine/islatravir treatment after week 144 up to week 192 (Part 4)

End point description:

An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study treatment, whether or not considered related to the study treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of a study treatment. The number of participants who experienced AEs during Part 4 are reported. Per protocol, all randomized participants who entered Part 4 and either continued treatment with DOR/ISL from Part 3 or switched

from DOR/3TC/TDF in Part 3 to DOR/ISL in Part 4; and received at least 1 dose of study treatment, corresponding to the study treatment they actually received were analyzed.

End point type	Secondary

End point timeframe:

Week 144 up to Week 192

End point values	DOR/ISL Continued (Part 4)	DOR/ISL Switch (Part 4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	67	22		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For All-Cause Mortality: from randomization up to 198 weeks. For AEs: from first treatment up to 198 weeks.

Adverse event reporting additional description:

The population analyzed for All-Cause Mortality was all randomized participants. The population analyzed for AEs was all randomized participants who received at least 1 dose of study treatment, corresponding to the study treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Islatravir 0.25mg

Reporting group description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144.

Reporting group title	Islatravir 0.75mg

Reporting group description:

In Part 1, participants were treated QD with 0.75 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 0.75 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144.

Reporting group title	Islatravir 2.25mg

Reporting group description:

In Part 1, participants were treated QD with 2.25 mg islatravir, 100 mg DOR, 300 mg 3TC, and placebo to DOR/3TC/TDF for a minimum of 24 weeks. In part 2, after receiving at least 24 weeks of study intervention, participants with HIV-1 RNA <50 copies/mL and no PDVF discontinued treatment of 3TC and placebo to DOR/3TC/TDF. Part 2 assessed ISL 2.25 mg (blind maintained) + DOR QD. After all participants had received at least 48 weeks of study intervention and the islatravir dose was selected, all participants in the islatravir group were switched to the selected dose 0.75 mg (between week 60 and week 84). Part 3 assessed Islatravir 0.75 mg + DOR QD open label through Week 144.

Reporting group title	DOR/3TC/TDF

Reporting group description:

In Part 1, participants were treated QD with placebo to islatravir, placebo to DOR, placebo to 3TC, and a fixed dose combination of DOR/3TC/TDF consisting of 100 mg DOR + 300 mg 3TC + 300 mg TDF for a minimum of 24 weeks. In Parts 2 and 3, after a minimum of 24 weeks of treatment, placebo treatments were discontinued and participants received only DOR/3TC/TDF QD open label up to Week 144.

Reporting group title	DOR/ISL Continued

Reporting group description:

In Part 4, beginning with week 144, participants who received the fixed dose combination of doravirine (100mg)/islatravir (0.75mg) QD open label in Part 3 and continued treatment through Week 192.

Reporting group title	DOR/ISL Switch

Reporting group description:

In Part 4, beginning with week 144, Participants who received DOR/3TC/TDF QD open label up to Week 144 were switched to the fixed dose combination of doravirine (100 mg)/islatravir (0.75 mg) QD open label and continued treatment until Week 192.

Serious adverse events	Islatravir 0.25mg	Islatravir 0.75mg	Islatravir 2.25mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 29 (6.90%)	6 / 30 (20.00%)	2 / 31 (6.45%)
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)			
Burkitt's lymphoma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 31 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (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
Congenital, familial and genetic disorders			
Long QT syndrome congenital			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (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
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (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
Blood and lymphatic system disorders			
Lymphadenopathy			

subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (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
Suicide attempt			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (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
Dysentery			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (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

Large intestine infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (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
Pneumonia chlamydial			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (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/3TC/TDF	DOR/ISL Continued	DOR/ISL Switch
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 31 (12.90%)	2 / 67 (2.99%)	1 / 22 (4.55%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Burkitt's lymphoma			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			

subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Long QT syndrome congenital			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Facial paralysis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			

subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (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			
Appendicitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (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
Dysentery			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia chlamydial			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary tuberculosis			

subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Islatravir 0.25mg	Islatravir 0.75mg	Islatravir 2.25mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 29 (75.86%)	26 / 30 (86.67%)	23 / 31 (74.19%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	2 / 31 (6.45%)
occurrences (all)	2	2	2
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 29 (3.45%)	4 / 30 (13.33%)	2 / 31 (6.45%)
occurrences (all)	1	4	2
Influenza like illness			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	1	0	1
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	4	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Oropharyngeal pain			
subjects affected / exposed	3 / 29 (10.34%)	3 / 30 (10.00%)	1 / 31 (3.23%)
occurrences (all)	3	3	3
Respiratory disorder			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	1	3	1
Rhinitis allergic			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Sneezing			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	3	0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 29 (3.45%)	3 / 30 (10.00%)	2 / 31 (6.45%)
occurrences (all)	1	4	2
Anxiety			
subjects affected / exposed	3 / 29 (10.34%)	6 / 30 (20.00%)	0 / 31 (0.00%)
occurrences (all)	3	7	0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Insomnia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	2	2	1
Weight increased			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 29 (6.90%)	1 / 30 (3.33%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Injury, poisoning and procedural complications			
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	3 / 31 (9.68%)
occurrences (all)	1	1	4
Sciatica			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	5 / 29 (17.24%)	2 / 30 (6.67%)	5 / 31 (16.13%)
occurrences (all)	5	5	6
Syncope			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	3
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Abdominal pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	2 / 31 (6.45%)
occurrences (all)	2	2	2
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	6 / 30 (20.00%)	3 / 31 (9.68%)
occurrences (all)	1	8	3
Aphthous ulcer			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Abdominal pain upper			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	2	2	1
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	5 / 30 (16.67%)	3 / 31 (9.68%)
occurrences (all)	1	6	3
Proctitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Vomiting			
subjects affected / exposed	3 / 29 (10.34%)	3 / 30 (10.00%)	2 / 31 (6.45%)
occurrences (all)	3	3	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 29 (10.34%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	4	3	2
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Penile ulceration			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	4 / 31 (12.90%)
occurrences (all)	1	2	4
Neck pain			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	3 / 31 (9.68%)
occurrences (all)	2	2	4
Pain in extremity			
subjects affected / exposed	3 / 29 (10.34%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	5	1	0
Osteopenia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	0	2	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 29 (6.90%)	7 / 30 (23.33%)	1 / 31 (3.23%)
occurrences (all)	3	7	1
Anal chlamydia infection			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	2	3	1
COVID-19			
subjects affected / exposed	0 / 29 (0.00%)	3 / 30 (10.00%)	1 / 31 (3.23%)
occurrences (all)	0	3	1
Cellulitis			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	2	0	2
Conjunctivitis			

subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
Escherichia urinary tract infection			
subjects affected / exposed	2 / 29 (6.90%)	1 / 30 (3.33%)	0 / 31 (0.00%)
occurrences (all)	2	1	0
Folliculitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	2
Fungal skin infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	1 / 31 (3.23%)
occurrences (all)	1	1	1
Influenza			
subjects affected / exposed	3 / 29 (10.34%)	1 / 30 (3.33%)	1 / 31 (3.23%)
occurrences (all)	3	1	1
Lower respiratory tract infection			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)	9 / 30 (30.00%)	2 / 31 (6.45%)
occurrences (all)	4	10	2
Oropharyngeal gonococcal infection			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	1	2	1
Oral herpes			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	3	2	1
Otitis media			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Paronychia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Pharyngitis			

subjects affected / exposed	1 / 29 (3.45%)	3 / 30 (10.00%)	0 / 31 (0.00%)
occurrences (all)	1	3	0
Proctitis gonococcal			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	2	2	1
Proctitis chlamydial			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 31 (3.23%)
occurrences (all)	0	2	1
Sinusitis			
subjects affected / exposed	4 / 29 (13.79%)	0 / 30 (0.00%)	0 / 31 (0.00%)
occurrences (all)	4	0	0
Syphilis			
subjects affected / exposed	6 / 29 (20.69%)	8 / 30 (26.67%)	2 / 31 (6.45%)
occurrences (all)	6	8	2
Tonsillitis			
subjects affected / exposed	2 / 29 (6.90%)	3 / 30 (10.00%)	1 / 31 (3.23%)
occurrences (all)	4	8	1
Tooth abscess			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	2 / 31 (6.45%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)	3 / 30 (10.00%)	3 / 31 (9.68%)
occurrences (all)	2	3	4
Urethritis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Viral pharyngitis			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 31 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	1 / 29 (3.45%)	6 / 30 (20.00%)	4 / 31 (12.90%)
occurrences (all)	1	6	4
Decreased appetite			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1

Non-serious adverse events	DOR/3TC/TDF	DOR/ISL Continued	DOR/ISL Switch
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 31 (70.97%)	21 / 67 (31.34%)	11 / 22 (50.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Fatigue			
subjects affected / exposed	3 / 31 (9.68%)	2 / 67 (2.99%)	0 / 22 (0.00%)
occurrences (all)	3	2	0
Influenza like illness			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Pyrexia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	2 / 31 (6.45%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	3	1	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	4	0	0
Oropharyngeal pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Respiratory disorder			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			

subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Sneezing			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Sinus congestion			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Depression			
subjects affected / exposed	3 / 31 (9.68%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	3	0	1
Anxiety			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	2 / 22 (9.09%)
occurrences (all)	1	0	2
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	3 / 31 (9.68%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	3	1	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	1 / 22 (4.55%)
occurrences (all)	0	1	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Procedural pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Headache			
subjects affected / exposed	4 / 31 (12.90%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	5	0	0
Syncope			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	2 / 31 (6.45%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	2	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	3 / 31 (9.68%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Diarrhoea			
subjects affected / exposed	8 / 31 (25.81%)	0 / 67 (0.00%)	3 / 22 (13.64%)
occurrences (all)	11	0	3
Aphthous ulcer			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0

Abdominal pain upper			
subjects affected / exposed	2 / 31 (6.45%)	2 / 67 (2.99%)	1 / 22 (4.55%)
occurrences (all)	2	2	1
Nausea			
subjects affected / exposed	3 / 31 (9.68%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	5	0	0
Proctitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	5	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Eczema			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Penile ulceration			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	3	0	0
Neck pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0

Back pain			
subjects affected / exposed	4 / 31 (12.90%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	4	0	1
Pain in extremity			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Osteopenia			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	5 / 31 (16.13%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	7	0	0
Anal chlamydia infection			
subjects affected / exposed	2 / 31 (6.45%)	2 / 67 (2.99%)	0 / 22 (0.00%)
occurrences (all)	2	2	0
COVID-19			
subjects affected / exposed	1 / 31 (3.23%)	2 / 67 (2.99%)	5 / 22 (22.73%)
occurrences (all)	1	2	5
Cellulitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Conjunctivitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Fungal skin infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Gastroenteritis			

subjects affected / exposed	4 / 31 (12.90%)	1 / 67 (1.49%)	1 / 22 (4.55%)
occurrences (all)	4	1	1
Influenza			
subjects affected / exposed	3 / 31 (9.68%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	4	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 31 (22.58%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	14	0	1
Oropharyngeal gonococcal infection			
subjects affected / exposed	1 / 31 (3.23%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	1	1	0
Oral herpes			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Otitis media			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Paronychia			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	4 / 31 (12.90%)	2 / 67 (2.99%)	0 / 22 (0.00%)
occurrences (all)	5	2	0
Proctitis gonococcal			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	1	0	1
Proctitis chlamydial			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 67 (0.00%)	1 / 22 (4.55%)
occurrences (all)	2	0	1
Syphilis			

subjects affected / exposed	6 / 31 (19.35%)	4 / 67 (5.97%)	1 / 22 (4.55%)
occurrences (all)	7	4	1
Tonsillitis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	3 / 31 (9.68%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	5	0	0
Urethritis			
subjects affected / exposed	0 / 31 (0.00%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Viral pharyngitis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 67 (1.49%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Vitamin D deficiency			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0
Decreased appetite			
subjects affected / exposed	2 / 31 (6.45%)	0 / 67 (0.00%)	0 / 22 (0.00%)
occurrences (all)	2	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 November 2017	Amendment 1: The primary purpose of the amendment was to incorporate several regulatory requests and correct/add several minor items.
27 March 2018	Amendment 2: The primary purpose of the amendment was to revise the safety follow-up period from ~14 days (2 weeks) to ~42 days (6 weeks) after the final dose of study treatment due to updated data which indicated the half-life of MK-8591 in plasma was expected to be between 87 and 128 hours after cessation of dosing for the dose range studied in this study. Therefore, a safety follow-up period of ~42 days was allowed for AE/SAE recording and reporting during this time.
15 November 2019	Amendment 3: The primary purpose of the amendment was to update the terminology in the protocol from "virologic failure" to "clinically significant confirmed viremia," which is consistent with clinical management of participants with HIV-1 and updated US DHHS guidelines. In addition, the study was extended to allow participants to receive an additional 24 weeks of open-label study treatment, and to collect additional safety and efficacy data. Thus, following Week 120, additional site visits were added at Week 132 and Week 144.
06 July 2020	Amendment 4: The primary purpose of the amendment was to extend the study for an additional 48 weeks (Part 4: 2-drug dosing with MK-8591A) to allow participants in Part 3 receiving the selected dose of MK-8591 in combination with DOR QD or MK-1439A in the control group to switch to a 2-drug fixed-dose combination (FDC) of MK-8591/DOR (referred to as MK-8591A) QD in Part 4, and to collect additional safety and efficacy data. MK-8591A was provided as open-label supplies. Additional site visits were added at Weeks 148, 156, 168, 180, and 192.
27 August 2020	Amendment 5: The primary purpose of the amendment was to remove the Week 120 interim analysis and to perform data analysis on an annual basis so that the next analysis would occur at Week 144.
31 January 2022	Amendment 6: The primary purpose of the amendment was 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 at the Week 192 visit in response to findings of decreases in CD4+ T-cell counts (in studies of participants with HIV) and lymphocytes (in studies of participants with or without HIV) in ISL clinical studies.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported