Clinical trial results:
A Phase 3 Randomized, Active-Controlled, Open-Label Clinical Study to Evaluate a Switch to Doravirine/Islatravir (DOR/ISL) Once-Daily in Participants With HIV-1 Virologically Suppressed on Antiretroviral Therapy

Summary

EudraCT number	2019-000586-20
Trial protocol	PL ES FR GB IT
Global end of trial date	26 August 2024

Results information

Result version number	v1 (current)
This version publication date	24 August 2025
First version publication date	24 August 2025

Trial information

Trial identification

Sponsor protocol code	MK-8591A-017

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04223778
WHO universal trial number (UTN)	-
Other trial identifiers	JAPIC-CTI: 205165

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@msd.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@msd.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	26 August 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 September 2021
Global end of trial reached?	Yes
Global end of trial date	26 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the safety and efficacy of a switch to MK-8591A (a fixed dose combination of doravirine and islatravir) in human immunodeficiency virus -1 (HIV-1)-infected participants virologically suppressed on a protocol-specified antiretroviral regimen. The primary hypothesis is that a switch to MK-8591A will be non-inferior to continued treatment with baseline antiretroviral therapy (ART) as assessed by the percentage of participants with HIV-1 ribonucleic acid (RNA) ≥50 copies/mL at Week 48.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 February 2020
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	33 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 20
Country: Number of subjects enrolled	Canada: 39
Country: Number of subjects enrolled	Chile: 31
Country: Number of subjects enrolled	Colombia: 31
Country: Number of subjects enrolled	France: 37
Country: Number of subjects enrolled	Italy: 37
Country: Number of subjects enrolled	Japan: 23
Country: Number of subjects enrolled	New Zealand: 7
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Russian Federation: 46
Country: Number of subjects enrolled	South Africa: 77
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	Switzerland: 65
Country: Number of subjects enrolled	United Kingdom: 36
Country: Number of subjects enrolled	United States: 143

Worldwide total number of subjects	672
EEA total number of subjects	154

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)	637
From 65 to 84 years	35
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult HIV-1-infected participants receiving baseline ART were enrolled in this study. 672 participants were randomly assigned in a 1:1 ratio to either Group 1: switch baseline ART to doravirine (DOR)/islatravir (ISL) on Day 1 to Week 96; or Group 2: continue baseline ART until Week 48 then switch to DOR/ISL from Week 48 to Week 96.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Doravirine/Islatravir (DOR/ISL)

Arm description:

Participants who were previously treated with continuous baseline antiretroviral therapy (ART) received DOR/ISL, a fixed dose combination (FDC) of 100 mg doravirine (DOR)/0.75 mg islatravir (ISL) orally once daily for 96 weeks.

Arm type	Experimental
Investigational medicinal product name	doravirine (DOR)/islatravir (ISL)
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

A fixed dose combination (FDC) of 100 mg DOR/ 0.75 mg ISL taken in tablet form, orally, once daily

Arm title	Group 2: Baseline Antiretroviral Therapy (ART)

Arm description:

Participants received continuous baseline ART for 48 weeks. Continuing participants delayed switch over from baseline ART to DOR/ISL, fixed dose combination of 100 mg DOR/0.75 mg ISL orally once daily, from Week 48 to Week 96, a total DOR/ISL treatment duration of 48 Weeks.

Arm type	Active comparator
Investigational medicinal product name	Baseline ART Regimen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Baseline ART regimen will be administered as per approved label. ART medication will not be provided by the Sponsor; participants will provide their own ART medications. Allowed drug classes include nucleoside analog reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transferase inhibitors (InSTIs), fusion inhibitors, chemokine receptor 5 (CCR5) antagonists, post-attachment inhibitor, and pharmacokinetic (PK) boosters.

Investigational medicinal product name	doravirine (DOR)/islatravir (ISL)
Investigational medicinal product code	
Other name	MK-8591A
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

A fixed dose combination (FDC) of 100 mg DOR/ 0.75 mg ISL taken in tablet form, orally, once daily

Number of subjects in period 1	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)
Started	336	336
Group 1 DOR/ISL Weeks 0-48	336	0 [1]
Group 1 DOR/ISL Weeks 48-96	322	0 [2]
Group 2 Baseline ART Weeks 0-48	0 [3]	336
Group 2 Switch to DOR/ISL Weeks 48-96	0 [4]	326
Completed	279	299
Not completed	57	37
Physician decision	10	6
Consent withdrawn by subject	35	17
Not Reported	7	8
Death	1	1
Lost to follow-up	4	5

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Per protocol, Group 1 DOR/ISL from Weeks 0-48 is not applicable to Group 2: Baseline ART arm.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Per protocol, Group 1 DOR/ISL from Weeks 48-96 is not applicable to Group 2: Baseline ART arm.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Per protocol, Group 2 Baseline ART from Weeks 0-48 is not applicable to Group 1: DOR/ISL arm.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Per protocol, Group 2 Baseline ART Switch to DOR/ISL is not applicable to Group 1: DOR/ISL arm.

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Doravirine/Islatravir (DOR/ISL)
Reporting group description:	
Participants who were previously treated with continuous baseline antiretroviral therapy (ART) received DOR/ISL, a fixed dose combination (FDC) of 100 mg doravirine (DOR)/0.75 mg islatravir (ISL) orally once daily for 96 weeks.	
Reporting group title	Group 2: Baseline Antiretroviral Therapy (ART)
Reporting group description:	
Participants received continuous baseline ART for 48 weeks. Continuing participants delayed switch over from baseline ART to DOR/ISL, fixed dose combination of 100 mg DOR/0.75 mg ISL orally once daily, from Week 48 to Week 96, a total DOR/ISL treatment duration of 48 Weeks.	

Reporting group values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)	Total
Number of subjects	336	336	672
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	321	316	637
From 65-84 years	15	20	35
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	45.5	45.4	
standard deviation	± 11.7	± 11.7	-
Sex: Female, Male Units: Participants			
Female	123	126	249
Male	213	210	423
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	4	8	12
Asian	19	19	38
Native Hawaiian or Other Pacific Islander	0	2	2
Black or African American	88	91	179
White	210	198	408
More than one race	13	16	29
Unknown or Not Reported	2	2	4
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	67	64	131

Not Hispanic or Latino	266	270	536
Unknown or Not Reported	3	2	5
ART Regimen Stratification			
Participants were stratified into the following baseline ART regimen: (1) Protease inhibitor (PI)-containing regimens (including PI- and integrase strand transferase inhibitor [InSTI]-containing regimens); (2) InSTI-based regimens (non-PI containing regimens); (3) All other non-PI- and non-InSTI containing regimens.			
Units: Subjects			
PI-regimens (both PI- & InSTI-containing regimens)	46	46	92
InSTI-based regimens (non-PI containing regimens)	174	174	348
All other non-PI- & non-InSTI containing regimens	116	116	232

End points

End points reporting groups

Reporting group title	Group 1: Doravirine/Islatravir (DOR/ISL)
Reporting group description:	
Participants who were previously treated with continuous baseline antiretroviral therapy (ART) received DOR/ISL, a fixed dose combination (FDC) of 100 mg doravirine (DOR)/0.75 mg islatravir (ISL) orally once daily for 96 weeks.	
Reporting group title	Group 2: Baseline Antiretroviral Therapy (ART)
Reporting group description:	
Participants received continuous baseline ART for 48 weeks. Continuing participants delayed switch over from baseline ART to DOR/ISL, fixed dose combination of 100 mg DOR/0.75 mg ISL orally once daily, from Week 48 to Week 96, a total DOR/ISL treatment duration of 48 Weeks.	

Primary: Percentage of Participants with Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) ≥50 copies/mL at Week 48

End point title	Percentage of Participants with Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) ≥50 copies/mL at Week 48
End point description:	
HIV-1 RNA levels in blood samples taken at each visit were measured by the Abbott RealTime polymerase chain reaction (PCR) assay with a reliable lower limit of quantification of 40 copies/mL. The percentage of participants with HIV-1 RNA ≥50 copies/mL at Week 48 is presented using the FDA Snapshot missing data approach. The analysis population consisted of all randomized participants who received at least one dose of study intervention.	
End point type	Primary
End point timeframe:	
Week 48	

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	336		
Units: Percentage of Participants				
number (not applicable)	0.0	1.5		

Statistical analyses

Statistical analysis title	Treatment Difference (Group 1 – Group 2)
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	672
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Estimated Difference
Point estimate	-1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.44
upper limit	-0.34

Notes:

[1] - Doravirine/Islatravir (DOR/ISL)- Baseline Antiretroviral Therapy (ART). Non-inferiority was concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI was less than 4 percentage points.

Primary: Percentage of Participants with one or more adverse events (AEs) up to Week 48

End point title	Percentage of Participants with one or more adverse events (AEs) up to Week 48

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who experienced at least one AE was reported. The analysis population consisted of all randomized participants who received at least one dose of study intervention.

End point type	Primary

End point timeframe:

Up to ~48 Weeks

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	336		
Units: Percentage of Participants				
number (not applicable)	80.1	70.2		

Statistical analyses

Statistical analysis title	Difference in percentage versus Baseline ART
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	672
Analysis specification	Pre-specified
Analysis type	other[2]
Parameter estimate	Estimated Difference
Point estimate	9.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	16.3

Notes:

[2] - Difference in percentage versus Baseline Antiretroviral Therapy (ART). Type of statistical test 'other' denotes no hypothesis testing was conducted.

Primary: Percentage of Participants who discontinued study intervention due to an AE up to Week 48

End point title	Percentage of Participants who discontinued study intervention due to an AE up to Week 48

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who discontinued study intervention due to an AE was reported. The analysis population consisted of all randomized participants who received at least one dose of study intervention.

End point type	Primary

End point timeframe:

Up to ~48 Weeks

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	336		
Units: Percentage of Participants				
number (not applicable)	2.1	0.3		

Statistical analyses

Statistical analysis title	Difference in percentage versus Baseline ART
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	672
Analysis specification	Pre-specified
Analysis type	other[3]
Parameter estimate	Estimated Difference
Point estimate	1.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	4

Notes:

[3] - Difference in percentage versus Baseline Antiretroviral Therapy (ART). Type of statistical test 'other' denotes no hypothesis testing was conducted.

Secondary: Percentage of Participants with HIV-1 RNA <40 or <50 copies/mL at Week 48

End point title	Percentage of Participants with HIV-1 RNA <40 or <50 copies/mL at Week 48

End point description:

HIV-1 RNA levels in blood samples taken at each visit were measured by the Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL. The percentage of participants with HIV-1 RNA <40 copies/mL or <50 copies/mL at Week 48 is presented using the FDA Snapshot missing data approach. The analysis population consisted of all randomized participants who received at least one dose of study intervention.

End point type	Secondary

End point timeframe:

Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	336		
Units: Percentage of Participants				
number (not applicable)				
HIV-1 RNA <40 copies/mL	94.6	94.3		
HIV-1 RNA <50 copies/mL	95.2	94.3		

Statistical analyses

Statistical analysis title	Treatment Difference (Group 1 – Group 2)

Statistical analysis description:

HIV-1 RNA <50 copies/mL

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	672
Analysis specification	Pre-specified
Analysis type	other[4]
Parameter estimate	Estimated Difference
Point estimate	0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.58
upper limit	4.43

Notes:

[4] - Doravirine/Islatravir (DOR/ISL)- Baseline Antiretroviral Therapy (ART). Type of statistical test 'other' denotes no hypothesis testing was conducted.

Statistical analysis title	Treatment Difference (Group 1 – Group 2)

Statistical analysis description:

HIV-1 RNA <40 copies/mL

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	672
Analysis specification	Pre-specified
Analysis type	other[5]
Parameter estimate	Estimated Difference
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.28
upper limit	3.9

Notes:

[5] - Doravirine/Islatravir (DOR/ISL) - Baseline Antiretroviral Therapy (ART). Type of statistical test 'other' denotes no hypothesis testing was conducted.

Secondary: Group 2 (Switch-Over): Percentage of Participants With HIV-1 RNA ≥50 Copies/mL, <40 Copies/mL or <50 Copies/mL at Week 96

End point title	Group 2 (Switch-Over): Percentage of Participants With HIV-1 RNA ≥50 Copies/mL, <40 Copies/mL or <50 Copies/mL at Week 96

End point description:

HIV-1 RNA levels in blood samples taken at each visit was measured by the Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL. The percentage of participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL, or <50 copies/mL at Week 96 is reported for Group 2 participants who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96. The analysis population consisted of all randomized participants in Group 2 who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96 who received at least one dose of study intervention and had data available for this outcome measure. Per protocol, the percentage of participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL, or <50 copies/mL at Week 96 for Group 1 participants is a separate outcome measure and is presented later in the record.

End point type	Secondary

End point timeframe:

Week 96

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[6]	326[7]		
Units: Percentage of Participants				
number (confidence interval 95%)				
HIV-1 RNA ≥50 copies/mL	(to)	0.9 (0.2 to 2.7)		
HIV-1 RNA <50 copies/mL	(to)	89.6 (85.7 to 92.7)		
HIV-1 RNA <40 copies/mL	(to)	89.6 (85.7 to 92.7)		

Notes:

[6] - Per protocol, this endpoint is for Group 2 only. Group 1 is presented in a separate endpoint.

[7] - Number of subjects analyzed is participants in Group 2 who delayed switch to DOR/ISL Weeks 48-96

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in CD4+ T-cell count at Week 48

End point title	Percentage change from baseline in CD4+ T-cell count at Week 48

End point description:

Plasma CD4+ T-Cell Count was measured in cells/mm^3 for baseline and 48 weeks. Baseline measurements were defined as the Day 1 value of each participant. The percentage change from baseline to Week 48 is presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and who have baseline data.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	313[8]	311[9]		
Units: Percentage Change				
arithmetic mean (confidence interval 95%)	-0.7 (-4.0 to 2.6)	8.7 (5.4 to 12.0)		

Notes:

[8] - Number of subjects analyzed is Group 1 treated participants with baseline data available

[9] - Number of subjects analyzed is Group 2 ART treated participants with baseline data available

Statistical analyses

Statistical analysis title	Difference in percentage versus Baseline ART
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	624
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	Estimated Difference
Point estimate	-8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.4
upper limit	-4.5

Notes:

[10] - Difference in percentage versus Baseline Antiretroviral Therapy (ART). Type of statistical test 'other' denotes no hypothesis testing was conducted.

Secondary: Group 1: Percentage of Participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL or <50 copies/mL at Week 96

End point title	Group 1: Percentage of Participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL or <50 copies/mL at Week 96

End point description:

HIV-1 RNA levels in blood samples taken at each visit was measured by the Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL. The percentage of participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL, or <50 copies/mL at Week 96 is reported for Group 1 participants. The analysis population consisted of all randomized participants in Group 1 who received at least one dose of study intervention and had data available for this outcome measure. Per protocol, the percentage of participants with HIV-1 RNA ≥50 copies/mL, <40 copies/mL, or <50 copies/mL at Week 96 for Group 2 participants who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96 is a separate outcome measure and is presented earlier in the record.

End point type	Secondary

End point timeframe:

Week 96

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	0[11]		
Units: Percentage of Participants				
number (confidence interval 95%)				
HIV-1 RNA ≥50 copies/mL	1.2 (0.3 to 3.0)	(to)		
HIV-1 RNA <40 copies/mL	86.0 (81.8 to 89.5)	(to)		
HIV-1 RNA <50 copies/mL	85.7 (81.5 to 89.3)	(to)		

Notes:

[11] - Per protocol, this endpoint is for Group 1 only. Group 2 is presented in a separate endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with evidence of viral drug resistance-associated substitutions at Week 96

End point title	Percentage of Participants with evidence of viral drug resistance-associated substitutions at Week 96

End point description:

Viral drug resistance was defined as participants with confirmed HIV-1 RNA ≥400 copies/mL and/or genotypic or phenotypic analysis of data showing evidence of resistance to the study drug administered. The percentage of participants who demonstrate drug resistance at Week 96 is presented for Group 1 and Group 2 participants who switched-over from baseline ART to receive DOR/ISL treatment from Week 48 to Week 96. The analysis population consisted of participants with virologic rebound (2 repeated incidents of HIV-1 RNA ≥200 copies/mL, 2-4 weeks apart) or who discontinued study intervention with HIV-1 RNA ≥200 copies/mL. Participants with available data showing resistance, despite viral load, are included. Per protocol, percentage of participants with evidence of viral drug resistance associated substitutions from week 0 to week 48 for Groups 1 and 2 is a separate outcome measure reported earlier in the record.

End point type	Secondary

End point timeframe:

Week 96

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	326[12]		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Notes:

[12] - Number of subjects analyzed is participants in Group 2 who delayed switch to DOR/ISL Weeks 48-96

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with evidence of viral drug resistance-associated substitutions at Week 48

End point title	Percentage of Participants with evidence of viral drug resistance-associated substitutions at Week 48

End point description:

Viral drug resistance is defined as participants with confirmed HIV-1 RNA ≥400 copies/mL and/or genotypic or phenotypic analysis of data showing evidence of resistance to the study drug administered. The percentage of participants who demonstrated drug resistance at Week 48 is presented. The analysis population consisted of participants who met the definition of confirmed virologic rebound (two consecutive [2 to 4 weeks apart] occurrences of HIV-1 RNA ≥200 copies/mL) at any time during the study or who discontinued study intervention for another reason and have HIV-1 RNA ≥200 copies/mL at the time of discontinuation. Participants for whom available genotypic or phenotypic data showed evidence of resistance, irrespective of viral load, were also included.

End point type	Secondary

End point timeframe:

Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	336		
Units: Percentage of Participants				
number (not applicable)	0.0	0.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Group 1 & Group 2 (Switch-Over): Percentage Change From Week 48 in CD4+ T-cell Count at Week 96

End point title	Group 1 & Group 2 (Switch-Over): Percentage Change From Week 48 in CD4+ T-cell Count at Week 96

End point description:

Plasma CD4+ T-Cell Count was measured in cells/mm^3 for Week 48 and Week 96. The mean percent change from Week 48 to Week 96 is reported for Group 1 and Group 2 participants who delayed switch over from baseline ART to DOR/ISL Week 48 to Week 96. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available for this outcome measure for participants in Group 1 and participants in Group 2 who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96.

End point type	Secondary

End point timeframe:

Week 48 and Week 96

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	289[13]	285[14]		
Units: Percentage Change				
arithmetic mean (confidence interval 95%)	5.29 (1.99 to 8.58)	0.16 (-2.96 to 3.29)		

Notes:

[13] - Number of subjects analyzed is Group 1 treated participants with data available

[14] - Number of subjects analyzed Group 2 DOR/ISL treated participants with data available Weeks 48-96

Statistical analyses

No statistical analyses for this end point

Secondary: Group 1: Percentage Change From Baseline in CD4+ T-cell Count at Week 96

End point title	Group 1: Percentage Change From Baseline in CD4+ T-cell Count at Week 96

End point description:

Plasma CD4+ T-Cell Count was measured in cells/mm^3 for baseline and 96 weeks. Baseline measurements were defined as the Day 1 value of each participant. The mean percent change from baseline to Week 96 in CD4+ T-cell count is reported for Group 1 participants. The analysis population consisted of all randomized participants in Group 1 who received at least one dose of study intervention and had data, including baseline data, available for this outcome measure. Per protocol, the percentage change from baseline in CD4+ T-cell count at Week 96 for Group 2 participants was not planned or conducted.

End point type	Secondary

End point timeframe:

Baseline and Week 96

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	284[15]	0[16]		
Units: Percentage Change				
arithmetic mean (confidence interval 95%)	4.49 (0.56 to 8.43)	(to)		

Notes:

[15] - Number of subjects analyzed is Group 1 treated participants with data available

[16] - Per protocol, this endpoint is for Group 1 only; Group 2 analysis was not planned or conducted.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to Week 24 in fasting lipids in participants on protease inhibitor (PI)-containing regimens (including PI- and integrase strand transferase inhibitor [InSTI]-containing regimens)

End point title	Change from baseline to Week 24 in fasting lipids in participants on protease inhibitor (PI)-containing regimens (including PI- and integrase strand transferase inhibitor [InSTI]-containing regimens)

End point description:

Blood serum samples were taken at baseline and Week 24. Per protocol, this outcome analysis was conducted in participants on PI-containing regimens (including PI- and InSTI-containing regimens), excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting high density lipoprotein (HDL) cholesterol, fasting low density lipoprotein (LDL) cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 24 in fasting lipids is presented. The analysis population consisted of all randomized participants on PI-containing regimens (including PI- and InSTI-containing regimens) who received at least one dose of study intervention and had baseline and Week 24 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32[17]	40[18]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=32, 40)	-12.94 (-23.94 to -1.94)	6.20 (-2.16 to 14.56)		
Fasting HDL (n=32, 40)	-0.97 (-5.94 to 4.00)	0.76 (-1.80 to 3.32)		
Fasting LDL Cholesterol (n=32, 40)	-7.47 (-15.86 to 0.92)	5.93 (-1.08 to 12.93)		
Fasting Non-HDL Cholesterol (n=32, 40)	-11.97 (-21.83 to -2.10)	5.44 (-2.29 to 13.16)		
Fasting Triglycerides (n=32, 40)	-22.69 (-42.92 to -2.46)	-3.16 (-19.81 to 13.49)		

Notes:

[17] - Number of subjects analyzed is Group 1 treated participants (PI-containing regimens) with data

[18] - Number of subjects analyzed is Group 2 ART treated participants (PI-containing regimens) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description: Fasting HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[19]
Parameter estimate	Estimated Difference
Point estimate	-1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.55
upper limit	3.84

Notes:

[19] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 32; Group 2: Baseline Antiretroviral Therapy (ART) n=40).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description: Fasting Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[20]
Parameter estimate	Estimated Difference
Point estimate	-19.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.07
upper limit	-6.44

Notes:

[20] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 32; Group 2: Baseline Antiretroviral Therapy (ART) n=40).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[21]
Parameter estimate	Estimated Difference
Point estimate	-17.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.02
upper limit	-5.46

Notes:

[21] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 32; Group 2: Baseline Antiretroviral Therapy (ART) n=40).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Triglycerides	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[22]
Parameter estimate	Estimated Difference
Point estimate	-21.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-45.51
upper limit	2.96

Notes:

[22] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 32; Group 2: Baseline Antiretroviral Therapy (ART) n=40).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description: Fasting LDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	72
Analysis specification	Pre-specified
Analysis type	other[23]
Parameter estimate	Estimated Difference
Point estimate	-13.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-24.69
upper limit	-3.2

Notes:

[23] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 32; Group 2: Baseline Antiretroviral Therapy (ART) n=40).

Secondary: Change from baseline to Week 24 in fasting lipids in participants on InSTI-based regimens (non-PI containing regimens)

End point title	Change from baseline to Week 24 in fasting lipids in participants on InSTI-based regimens (non-PI containing regimens)

End point description:

Blood serum samples were taken at baseline and Week 24. Per protocol, this outcome analysis was conducted in participants on InSTI-based regimens (non-PI containing regimens), excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting HDL cholesterol, fasting LDL cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 24 in fasting lipids is presented. The analysis population consisted of all randomized participants on InSTI-based regimens (non-PI containing regimens) who received at least one dose of study intervention and had baseline and Week 24 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	130[24]	135[25]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=130, 135)	2.98 (-2.19 to 8.14)	8.74 (4.25 to 13.23)		
Fasting HDL Cholesterol (n=130, 135)	0.84 (-1.11 to 2.79)	0.27 (-1.06 to 1.60)		
Fasting LDL Cholesterol (n=128, 135)	3.21 (-1.49 to 7.92)	8.50 (4.27 to 12.73)		
Fasting Non-HDL Cholesterol (n=130, 135)	2.14 (-3.39 to 7.67)	8.47 (4.05 to 12.90)		

Fasting Triglycerides (n=130, 135)	-0.97 (-17.98 to 16.04)	-1.56 (-10.80 to 7.69)		

Notes:

[24] - Number of subjects analyzed is Group 1 treated participants (InSTI-containing regimens) with data
[25] - Number of subjects analyzed Group 2 ART treated participants (InSTI-containing regimens) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	other[26]
Parameter estimate	Estimated Difference
Point estimate	-4.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.43
upper limit	2.09

Notes:

[26] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 130; Group 2: Baseline Antiretroviral Therapy (ART) n=135).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Triglycerides	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	other[27]
Parameter estimate	Estimated Difference
Point estimate	1.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-16.14
upper limit	19.43

Notes:

[27] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 130; Group 2: Baseline Antiretroviral Therapy (ART) n=135).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	other[28]
Parameter estimate	Estimated Difference
Point estimate	-4.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.21
upper limit	1.38

Notes:

[28] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 130; Group 2: Baseline Antiretroviral Therapy (ART) n=135).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	other[29]
Parameter estimate	Estimated Difference
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	3.09

Notes:

[29] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 130; Group 2: Baseline Antiretroviral Therapy (ART) n=135).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting LDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	265
Analysis specification	Pre-specified
Analysis type	other[30]
Parameter estimate	Estimated Difference
Point estimate	-3.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.47
upper limit	1.74

Notes:

[30] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n= 128; Group 2: Baseline Antiretroviral Therapy (ART) n=135).

Secondary: Change from baseline to Week 24 in fasting lipids in participants on all other non-PI- and non-InSTI containing regimens

End point title	Change from baseline to Week 24 in fasting lipids in participants on all other non-PI- and non-InSTI containing regimens

End point description:

Blood serum samples were taken at baseline and Week 24. Per protocol, this outcome analysis was conducted in participants on all other non-PI- and non-InSTI containing regimens, excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting HDL cholesterol, fasting LDL cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 24 in fasting lipids is presented. The analysis population consisted of all randomized participants on all other non-PI- and non-InSTI containing regimens, who received at least one dose of study intervention and had baseline and Week 24 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 24

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89[31]	95[32]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=89, 95)	7.18 (-0.49 to 14.85)	7.35 (2.44 to 12.25)		
Fasting HDL Cholesterol (n=88, 95)	-3.43 (-6.51 to -0.36)	-0.72 (-3.02 to 1.58)		
Fasting LDL Cholesterol (n=87, 95)	11.33 (5.75 to 16.92)	7.19 (3.35 to 11.04)		
Fasting Non-HDL Cholesterol (n=88, 95)	11.07 (4.40 to 17.74)	8.07 (4.10 to 12.04)		
Fasting Triglycerides (n=88, 95)	-1.16 (-14.27 to 11.95)	4.45 (-3.89 to 12.80)		

Notes:

[31] - Number of subjects analyzed is Group 1 treated participants (non-PI/non-InSTI) with data

[32] - Number of subjects analyzed is Group 2 ART treated participants (non-PI/non-InSTI) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART

Statistical analysis description:

Fasting HDL Cholesterol

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[33]
Parameter estimate	Estimated Difference
Point estimate	-3.16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.37
upper limit	0.05

Notes:

[33] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=88; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[34]
Parameter estimate	Estimated Difference
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.6
upper limit	9.7

Notes:

[34] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=89; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[35]
Parameter estimate	Estimated Difference
Point estimate	3.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.93
upper limit	11.19

Notes:

[35] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=88; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Triglycerides	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[36]
Parameter estimate	Estimated Difference
Point estimate	-1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.89
upper limit	12.31

Notes:

[36] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=88; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART

Statistical analysis description:

Fasting LDL Cholesterol

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	184
Analysis specification	Pre-specified
Analysis type	other[37]
Parameter estimate	Estimated Difference
Point estimate	4.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.27
upper limit	11.03

Notes:

[37] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=87; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Secondary: Change from baseline to Week 48 in fasting lipids in participants on protease inhibitor (PI)-containing regimens (including PI- and integrase strand transferase inhibitor [InSTI]-containing regimens)

End point title	Change from baseline to Week 48 in fasting lipids in participants on protease inhibitor (PI)-containing regimens (including PI- and integrase strand transferase inhibitor [InSTI]-containing regimens)

End point description:

Blood serum samples were taken at baseline and Week 48. Per protocol, this outcome analysis was conducted in participants on PI-containing regimens (including PI- and InSTI-containing regimens), excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting high density lipoprotein (HDL) cholesterol, fasting low density lipoprotein (LDL) cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 48 in fasting lipids is presented. The analysis population consisted of all randomized participants on PI-containing regimens (including PI- and InSTI-containing regimens) who received at least one dose of study intervention and had baseline and Week 48 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[38]	37[39]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=29, 37)	-15.31 (-28.99 to -1.64)	1.84 (-5.70 to 9.38)		
Fasting HDL Cholesterol (n=29, 36)	-1.45 (-6.01 to 3.11)	-1.08 (-3.91 to 1.75)		
Fasting LDL Cholesterol (n=29, 35)	-8.59 (-19.72 to 2.54)	3.37 (-3.30 to 10.04)		
Fasting Non-HDL Cholesterol (n=29, 36)	-13.86 (-25.28 to -2.45)	2.81 (-4.40 to 10.01)		
Fasting Triglycerides (n=29, 36)	-26.90 (-42.31 to -11.48)	2.28 (-16.39 to 20.95)		

Notes:

[38] - Number of subjects analyzed is Group 1 treated participants (PI-containing regimens) with data

[39] - Number of subjects analyzed is Group 2 ART treated participants (PI-containing regimens) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description: Fasting Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[40]
Parameter estimate	Estimated Difference
Point estimate	-18.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.05
upper limit	-4.76

Notes:

[40] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=37).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description: Fasting LDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[41]
Parameter estimate	Estimated Difference
Point estimate	-14.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-25.81
upper limit	-2.43

Notes:

[41] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=35).

Statistical analysis title	Fasting Non-HDL Cholesterol Multiplicity Adjusted

Statistical analysis description:

Treatment Difference vs Baseline ART. Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI is less than 0 percentage points. The multiplicity adjusted 95% CIs for treatment difference were calculated from ANCOVA models with terms for baseline measurement and treatment. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=36).

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0021 [42]
Method	ANCOVA
Parameter estimate	Median difference (net)
Point estimate	-18.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-32.28
upper limit	-4.17

Notes:

[42] - The significance level in model was ANCOVA 0.02497/2=0.012485. The p-value is statistically significant if it is <0.02497/2=0.012485.

Statistical analysis title	Treatment Difference versus Baseline ART

Statistical analysis description:

Fasting Triglycerides

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[43]
Parameter estimate	Estimated Difference
Point estimate	-27.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	-51.08
upper limit	-4.49

Notes:

[43] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=36).

Statistical analysis title	Treatment Difference vs Baseline ART
Statistical analysis description:	
Fasting LDL Cholesterol - Multiplicity Adjusted	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.0094 [45]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-14.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-27.56
upper limit	-0.68

Notes:

[44] - Treatment Difference vs Baseline ART. Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI is less than 0 percentage points. The multiplicity adjusted 95% CIs for treatment difference were calculated from ANCOVA models with terms for baseline measurement and treatment. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=35).

[45] - The significance level in ANCOVA model was 0.02497/2=0.012485. The p-value is statistically significant if it is <0.02497/2=0.012485.

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[46]
Parameter estimate	Estimated Difference
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	5.08

Notes:

[46] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=36).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	other[47]
Parameter estimate	Estimated Difference
Point estimate	-18.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.45
upper limit	-6

Notes:

[47] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=29; Group 2: Baseline Antiretroviral Therapy (ART) n=36).

Secondary: Change from baseline to Week 48 in fasting lipids in participants on InSTI-based regimens (non-PI containing regimens)

End point title	Change from baseline to Week 48 in fasting lipids in participants on InSTI-based regimens (non-PI containing regimens)

End point description:

Blood serum samples were taken at baseline and Week 48. Per protocol, this outcome analysis was conducted in participants on InSTI-based regimens (non-PI containing regimens), excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting HDL cholesterol, fasting LDL cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 48 in fasting lipids is presented. The analysis population consisted of all randomized participants on InSTI-based regimens (non-PI containing regimens) who received at least one dose of study intervention and had baseline and Week 48 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129[48]	137[49]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=129, 137)	2.23 (-2.70 to 7.17)	4.39 (-0.19 to 8.96)		
Fasting HDL Cholesterol (n=129, 136)	0.23 (-1.61 to 2.08)	0.13 (-1.24 to 1.51)		
Fasting LDL Cholesterol (n=129, 133)	2.74 (-1.27 to 6.76)	3.44 (-0.88 to 7.76)		
Fasting Non-HDL Cholesterol (n=129, 136)	2.00 (-3.16 to 7.16)	4.37 (-0.24 to 8.98)		
Fasting Triglycerides (n=129, 136)	-2.29 (-15.02 to 10.44)	4.44 (-5.60 to 14.48)		

Notes:

[48] - Number of subjects analyzed is Group 1 treated participants (non-PI/-InSTI) with data

[49] - Number of subjects analyzed is Group 2 ART treated participants (non-PI/-InSTI) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other[50]
Parameter estimate	Estimated Difference
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.26
upper limit	6.18

Notes:

[50] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=137).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other[51]
Parameter estimate	Estimated Difference
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.84
upper limit	2.54

Notes:

[51] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=136).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting LDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other[52]
Parameter estimate	Estimated Difference
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.83
upper limit	6.11

Notes:

[52] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=133).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other[53]
Parameter estimate	Estimated Difference
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.81
upper limit	5.83

Notes:

[53] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=136).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Triglycerides	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	other[54]
Parameter estimate	Estimated Difference
Point estimate	-5.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-20.46
upper limit	9.57

Notes:

[54] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=136).

Statistical analysis title	Treatment Difference vs Baseline ART
Statistical analysis description:	
Fasting LDL Cholesterol - Multiplicity Adjusted	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority[55]
P-value	= 0.4093 [56]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	0.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.63
upper limit	6.9

Notes:

[55] - Treatment Difference vs Baseline ART. Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI is less than 0 percentage points. The multiplicity adjusted 95% CIs for treatment difference were calculated from ANCOVA models with terms for baseline measurement and treatment. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=133).
[56] - The significance level in ANCOVA model was 0.02497/2=0.012485. The p-value is statistically significant if it is <0.02497/2=0.012485.

Statistical analysis title	Treatment Difference vs Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol - Multiplicity Adjusted	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	266
Analysis specification	Pre-specified
Analysis type	superiority[57]
P-value	= 0.4397 [58]
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.72
upper limit	6.75

Notes:

[57] - Treatment Difference vs Baseline ART. Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI is less than 0 percentage points. The multiplicity adjusted 95% CIs for treatment difference were calculated from ANCOVA models with terms for baseline measurement and treatment. Group 1: Doravirine/Islatravir (DOR/ISL) n=129; Group 2: Baseline Antiretroviral Therapy (ART) n=136).
[58] - The significance level in ANCOVA model was 0.02497/2=0.012485. The p-value is statistically significant if it is <0.02497/2=0.012485.

Secondary: Change from baseline to Week 48 in fasting lipids in participants on all other non-PI- and non-InSTI containing regimens

End point title	Change from baseline to Week 48 in fasting lipids in participants on all other non-PI- and non-InSTI containing

	regimens

End point description:

Blood serum samples were taken at baseline and Week 48. Per protocol, this outcome analysis was conducted in participants on all other non-PI- and non-InSTI containing regimens, excluding participants who took lipid-lowering therapy during the study. The fasting lipids consisted of fasting cholesterol, fasting HDL cholesterol, fasting LDL cholesterol, fasting non-HDL cholesterol, and fasting triglycerides. The mean change from baseline to Week 48 in fasting lipids is presented. The analysis population consisted of all randomized participants on all other non-PI- and non-InSTI containing regimens, who received at least one dose of study intervention and had baseline and Week 48 data available for each lipid type, excluding participants who took lipid-lowering therapy during the study, per protocol.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	91[59]	95[60]		
Units: mg/dL				
arithmetic mean (confidence interval 95%)				
Fasting Cholesterol (n=91, 95)	5.66 (-1.38 to 12.70)	4.62 (0.10 to 9.15)		
Fasting HDL Cholesterol (n=90, 95)	-3.84 (-6.72 to -0.97)	-1.98 (-4.60 to 0.63)		
Fasting LDL Cholesterol (n=90, 94)	9.27 (4.05 to 14.49)	7.30 (3.97 to 10.63)		
Fasting Non-HDL Cholesterol (n=90, 95)	9.94 (4.16 to 15.73)	6.61 (3.13 to 10.08)		
Fasting Triglycerides (n=90, 95)	3.33 (-9.54 to 16.21)	-2.97 (-12.37 to 6.43)		

Notes:

[59] - Number of subjects analyzed is Group 1 treated participants (non-PI/non-InSTI) with data

[60] - Number of subjects analyzed is Group 2 ART treated participants (non-PI/non-InSTI) with data

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART

Statistical analysis description:

Fasting Cholesterol

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[61]
Parameter estimate	Estimated Difference
Point estimate	2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.54
upper limit	10.17

Notes:

[61] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=91; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Triglycerides	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[62]
Parameter estimate	Estimated Difference
Point estimate	10.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.97
upper limit	24.96

Notes:

[62] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=90; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting Non-HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[63]
Parameter estimate	Estimated Difference
Point estimate	3.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	10.56

Notes:

[63] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=90; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART
Statistical analysis description:	
Fasting HDL Cholesterol	
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)

Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[64]
Parameter estimate	Estimated Difference
Point estimate	-2.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.69
upper limit	0.65

Notes:

[64] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=90; Group 2: Baseline Antiretroviral Therapy (ART) n=95).

Statistical analysis title	Treatment Difference versus Baseline ART

Statistical analysis description:

Fasting LDL Cholesterol

Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	other[65]
Parameter estimate	Estimated Difference
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.73
upper limit	8.42

Notes:

[65] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted. Group 1: Doravirine/Islatravir (DOR/ISL) n=90; Group 2: Baseline Antiretroviral Therapy (ART) n=94).

Secondary: Group 1: Percentage of Participants Who Discontinued Study Intervention Due to an AE up to Week 96

End point title	Group 1: Percentage of Participants Who Discontinued Study Intervention Due to an AE up to Week 96

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who discontinued study intervention due to an AE up to Week 96 is reported for Group 1 participants. The analysis population consisted of all randomized participants in Group 1 who received at least one dose of study intervention. Per protocol, the percentage of participants who discontinued study intervention for Group 2 participants is a separate outcome measure and is presented later in the record.

End point type	Secondary

End point timeframe:

Up to ~96 Weeks

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	0[66]		
Units: Percentage of Participants				
number (not applicable)	5.7			

Notes:

[66] - Per protocol, this endpoint is for Group 1 only. Group 2 is presented in a separate endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Group 1: Percentage of Participants With One or More AEs up to Week 96

End point title	Group 1: Percentage of Participants With One or More AEs up to Week 96

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who experienced at least one AE up to Week 96 is reported for Group 1 participants. The analysis population consisted of all randomized participants in Group 1 who received at least one dose of study intervention. Per protocol, the percentage of participants with one or more AEs for Group 2 participants is a separate outcome measure and is presented later in the record.

End point type	Secondary

End point timeframe:

Up to ~96 Weeks

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	336	0[67]		
Units: Percentage of Participants				
number (not applicable)	92.3			

Notes:

[67] - Per protocol, this endpoint is for Group 1 only. Group 2 is presented in a separate endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in body weight at Week 48 for InSTI-based regimens (non-PI-containing regimens)

End point title	Change from baseline in body weight at Week 48 for InSTI-based regimens (non-PI-containing regimens)

End point description:

Baseline measurements were defined as the Day 1 value of each participant. The change from baseline in body weight to Week 48 is presented for participants who received InSTI- based regimens. The

analysis population consisted of all randomized participants who received at least one dose of study intervention, had baseline and Week 48 data available for body weight, and received InSTI-based regimens.

End point type	Secondary

End point timeframe:

Baseline and Week 48

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	167[68]	169[69]		
Units: kg				
arithmetic mean (confidence interval 95%)	0.66 (-0.17 to 1.48)	0.10 (-0.56 to 0.75)		

Notes:

[68] - Number of subjects analyzed is Group 1 treated participants (InSTI) with data available

[69] - Number of subjects analyzed is Group 2 ART treated participants (InSTI) with data available

Statistical analyses

Statistical analysis title	Treatment Difference versus Baseline ART
Comparison groups	Group 1: Doravirine/Islatravir (DOR/ISL) v Group 2: Baseline Antiretroviral Therapy (ART)
Number of subjects included in analysis	336
Analysis specification	Pre-specified
Analysis type	other[70]
Parameter estimate	Estimated Difference
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	1.46

Notes:

[70] - Treatment Difference vs Baseline ART. Type of statistical test 'other' denotes no hypothesis testing was conducted.

Secondary: Group 1 & Group 2 (Switch-Over): Percentage of Participants who discontinued study intervention due to an AE from Week 48 to Week 96

End point title	Group 1 & Group 2 (Switch-Over): Percentage of Participants who discontinued study intervention due to an AE from Week 48 to Week 96

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who discontinued study intervention due to an AE from Week 48 up to Week 96 is reported for Group 1 participants and Group 2 participants who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96. The analysis population consisted of all randomized participants who received at least one dose of study intervention for participants in Group 1 and participants in Group 2 who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96.

End point type	Secondary

End point timeframe:

Weeks 48-96 (up to ~48 weeks)

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	322[71]	326[72]		
Units: Percentage of Participants				
number (not applicable)	3.7	2.5		

Notes:

[71] - Number of Subjects Analyzed is Group 1 participants who received DOR/ISL from 48-96 Weeks

[72] - Number of Subjects Analyzed is Group 2 participants who delayed switch over to DOR/ISL Weeks 48-96

Statistical analyses

No statistical analyses for this end point

Secondary: Group 1 & Group 2 (Switch-Over): Percentage of Participants With One or More AEs From Week 48 to Week 96

End point title	Group 1 & Group 2 (Switch-Over): Percentage of Participants With One or More AEs From Week 48 to Week 96

End point description:

An AE was defined as any untoward medical occurrence in a clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. The percentage of participants who experienced at least one AE from Week 48 up to Week 96 is reported for Group 1 participants and Group 2 participants who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96. The analysis population consisted of all randomized participants who received at least one dose of study intervention for participants in Group 1 and participants in Group 2 who delayed switch over from baseline ART to DOR/ISL from Week 48 to Week 96.

End point type	Secondary

End point timeframe:

Weeks 48-96 (up to ~48 weeks)

End point values	Group 1: Doravirine/Islatravir (DOR/ISL)	Group 2: Baseline Antiretroviral Therapy (ART)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	322[73]	326[74]		
Units: Percentage of Participants				
number (not applicable)	73.0	76.4		

Notes:

[73] - Number of Subjects Analyzed is Group 1 participants who received DOR/ISL from 48-96 Weeks

[74] - Number of Subjects Analyzed is Group 2 participants who delayed switch over to DOR/ISL Weeks 48-96

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to approximately 49 months

Adverse event reporting additional description:

All cause mortality (ACM): all randomized participants; AEs: all randomized participants who got ≥1 dose of study drug. Reported separately by Weeks 0-48 & 48-End of Trial. Per protocol, pregnancy related AEs & infant serious AEs collected for enrolled pregnant participants; included by participant arm. 1 infant AE death; & not reported for privacy

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Group 1: DOR/ISL Weeks 0-48
Reporting group description: -	
Reporting group title	Group 2: DOR/ISL Weeks 48-End of Trial
Reporting group description: -	
Reporting group title	Group 2: Baseline ART Weeks 0-48
Reporting group description: -	
Reporting group title	Group 1: DOR/ISL Weeks 48-End of Trial

Reporting group description: -

Serious adverse events	Group 1: DOR/ISL Weeks 0-48	Group 2: DOR/ISL Weeks 48-End of Trial	Group 2: Baseline ART Weeks 0-48
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 336 (4.76%)	12 / 326 (3.68%)	15 / 336 (4.46%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Pancreatic carcinoma			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Renal cancer			

subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Basal cell carcinoma			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Pregnancy, puerperium and perinatal conditions			
Premature delivery			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Abortion spontaneous			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Premature baby			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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			
Non-cardiac chest pain			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			

subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Lung disorder			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Asthma			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Psychiatric disorders			
Paranoia			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Major depression			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Troponin increased			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Lipase increased			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Ligament rupture			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Animal bite			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Post procedural haematoma			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Tibia fracture			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Extrasystoles			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Nervous system disorders			
Epilepsy			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Encephalopathy neonatal			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Neuralgic amyotrophy			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
VIth nerve paralysis			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Duodenal perforation			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Enterocolitis			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Inguinal hernia			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Calculus urinary			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Cervical spinal stenosis			

subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Intervertebral disc protrusion			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Osteoarthritis			
subjects affected / exposed	3 / 336 (0.89%)	0 / 326 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Chronic tonsillitis			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmodium falciparum infection			

subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Peritoneal abscess			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Omphalitis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Malaria			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	0 / 336 (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
Infectious pleural effusion			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 336 (0.00%)	1 / 326 (0.31%)	0 / 336 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 336 (0.30%)	0 / 326 (0.00%)	0 / 336 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 336 (0.00%)	0 / 326 (0.00%)	1 / 336 (0.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 1: DOR/ISL Weeks 48-End of Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 322 (4.04%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Hodgkin's disease			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal cancer			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			

subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Premature delivery			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Premature baby			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Lung disorder			

subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Paranoia			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Troponin increased			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lipase increased			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Hand fracture			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Ligament rupture			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Animal bite			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Foot fracture			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Post procedural haematoma			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Road traffic accident			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Extrasystoles			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Epilepsy			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Encephalopathy neonatal			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neuralgic amyotrophy			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
VIth nerve paralysis			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphadenitis			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Duodenal perforation			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Enterocolitis				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Calculus urinary				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal colic				
subjects affected / exposed	1 / 322 (0.31%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthritis				
subjects affected / exposed	1 / 322 (0.31%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cervical spinal stenosis				
subjects affected / exposed	1 / 322 (0.31%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	1 / 322 (0.31%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Osteoarthritis			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 322 (0.31%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal abscess			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chronic tonsillitis			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Plasmodium falciparum infection			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peritoneal abscess			
subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Omphalitis			

subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaria				
subjects affected / exposed	1 / 322 (0.31%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infectious pleural effusion				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal bacteraemia				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tonsillitis				
subjects affected / exposed	0 / 322 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hypoglycaemia				

subjects affected / exposed	0 / 322 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1: DOR/ISL Weeks 0-48	Group 2: DOR/ISL Weeks 48-End of Trial	Group 2: Baseline ART Weeks 0-48
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 336 (25.30%)	120 / 326 (36.81%)	52 / 336 (15.48%)
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 336 (0.00%)	44 / 326 (13.50%)	0 / 336 (0.00%)
occurrences (all)	0	46	0
CD4 lymphocytes decreased			
subjects affected / exposed	2 / 336 (0.60%)	39 / 326 (11.96%)	0 / 336 (0.00%)
occurrences (all)	2	41	0
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	24 / 336 (7.14%)	8 / 326 (2.45%)	3 / 336 (0.89%)
occurrences (all)	28	12	4
Nervous system disorders			
Headache			
subjects affected / exposed	36 / 336 (10.71%)	14 / 326 (4.29%)	16 / 336 (4.76%)
occurrences (all)	41	14	17
Musculoskeletal and connective tissue disorders			
Osteopenia			
subjects affected / exposed	10 / 336 (2.98%)	7 / 326 (2.15%)	19 / 336 (5.65%)
occurrences (all)	10	7	19
Infections and infestations			
COVID-19			
subjects affected / exposed	18 / 336 (5.36%)	57 / 326 (17.48%)	15 / 336 (4.46%)
occurrences (all)	19	60	16

Non-serious adverse events	Group 1: DOR/ISL Weeks 48-End of Trial		
Total subjects affected by non-serious			

adverse events subjects affected / exposed	115 / 322 (35.71%)		
Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all) CD4 lymphocytes decreased subjects affected / exposed occurrences (all)	 65 / 322 (20.19%) 70 45 / 322 (13.98%) 47		
Injury, poisoning and procedural complications Accidental overdose subjects affected / exposed occurrences (all)	 4 / 322 (1.24%) 4		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	 12 / 322 (3.73%) 14		
Musculoskeletal and connective tissue disorders Osteopenia subjects affected / exposed occurrences (all)	 2 / 322 (0.62%) 2		
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	 42 / 322 (13.04%) 42		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 June 2020	Amendment 02: The protocol was amended to: (1) allow participants to rescreen one time following approval from the Sponsor, and (2) add a scheduled study visit at Week 52 so that participants in Group 2 can be monitored 4 weeks after switching to DOR/ISL.
15 January 2021	Amendment 03: The main reasons the protocol was amended were to: (1) permit continued administration of study intervention in participants who become pregnant (where allowed by local regulations and as appropriate based on available data/local standard of-care guidelines), (2) add a discontinuation criterion if a participant chooses to breastfeed, and (3) update dose modification instructions.
12 May 2021	Amendment 04: Additional pharmacokinetics (PK) sampling and increased safety monitoring for participants who become pregnant and continue study intervention. Increased safety data collection for infants born to participants who become pregnant.
26 January 2022	Amendment 05: To increase frequency of monitoring of CD4+ T-cell counts and lymphocyte counts, and to add discontinuation criteria 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. Note: The changes made in Amendment 05 were not implemented at clinical sites. Amendment 06 supersedes Amendment 05.
16 February 2022	Amendment 06: Given the findings of decreases in CD4+ T-cell and total lymphocyte counts in clinical studies evaluating ISL, the protocol is being amended to increase the frequency of monitoring of CD4+ T-cell and total lymphocyte counts and to specify the management of participants who meet protocol-defined decreases in CD4+ T-cell and/or total lymphocyte counts.
08 December 2022	Amendment 08: Merck Sharp & Dohme Corp. underwent an entity name and address change to Merck Sharp & Dohme LLC, Rahway, NJ, USA. This conversion resulted only in an entity name change and update to the address.
24 April 2024	Amendment 09: The protocol was amended to revise the post-treatment management of participants with specific decreases in CD4+ T-cell or total lymphocyte counts. The recovery criteria were revised to account for normal physiologic variability in CD4+ T-cell or total lymphocyte counts and the frequency of monitoring was updated to minimize the burden on study participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported