# Clinical trial results:
# A Phase 3 Randomized, Active-Controlled, Double-Blind Clinical Study to Evaluate the Antiretroviral Activity, Safety, and Tolerability of Doravirine/Islatravir Once-Daily in HIV-1 Infected Treatment-Naïve Participants

## Summary

| | |
|---|---|
| EudraCT number | 2019-000590-23 |
| Trial protocol | ES FR DE IT |
| Global end of trial date | 29 January 2025 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 25 January 2026 |
| First version publication date | 25 January 2026 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MK-8591A-020 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04233879 |
| WHO universal trial number (UTN) | - |
| Other trial identifiers | jRCT: jRCT2031210024 |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Merck Sharp & Dohme LLC |
| Sponsor organisation address | 126 East Lincoln Avenue, P.O. Box 2000, Rahway, 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 | 29 January 2025 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 November 2022 |
| Global end of trial reached? | Yes |
| Global end of trial date | 29 January 2025 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

This is a phase 3, randomized, controlled, double-blind, multisite clinical study of a once-daily fixed dose combination (FDC) of 100 mg doravirine/0.75 mg islatravir (DOR/ISL [also known as MK-8591A]) in treatment-naïve participants living with human immunodeficiency virus type-1 (HIV-1) infection. The primary objectives are to evaluate the antiretroviral activity, safety, and tolerability of DOR/ISL compared to bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF). The primary hypothesis is that DOR/ISL is noninferior or superior to BIC/FTC/TAF treatment based on 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 | 28 February 2020 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 27 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 35 |
| Country: Number of subjects enrolled | Canada: 23 |
| Country: Number of subjects enrolled | Chile: 67 |
| Country: Number of subjects enrolled | Colombia: 37 |
| Country: Number of subjects enrolled | France: 41 |
| Country: Number of subjects enrolled | Germany: 26 |
| Country: Number of subjects enrolled | Israel: 23 |
| Country: Number of subjects enrolled | Italy: 31 |
| Country: Number of subjects enrolled | Japan: 16 |
| Country: Number of subjects enrolled | South Africa: 108 |
| Country: Number of subjects enrolled | Spain: 76 |
| Country: Number of subjects enrolled | Taiwan: 4 |
| Country: Number of subjects enrolled | United States: 112 |

| | |
|---|---|
| Worldwide total number of subjects | 599 |
| EEA total number of subjects | 174 |

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) | 594 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Treatment-naïve participants living with Human Immunodeficiency Virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy were enrolled.

### Pre-assignment

Screening details:

A total of 599 participants were randomized in the study and 597 received at least 1 dose of study intervention. The safety analyses were conducted using all participants as treated population, which included all randomized participants who received at least 1 dose of study intervention.

### Period 1

| | |
|---|---|
| Period 1 title | Base Study (Day 1 to Week 144) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1: DOR/ISL |

Arm description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| 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:

100 mg DOR/0.75 mg ISL fixed dose combination (FDC) single tablet taken once daily by mouth.

| | |
|---|---|
| Investigational medicinal product name | Placebo to fixed dose combination (FDC) DOR/ISL |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo to FDC DOR/ISL in a single tablet taken orally, once daily

| | |
|---|---|
| Investigational medicinal product name | Placebo to BIC/FTC/TAF |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo to BIC/FTC/TAF in a single tablet taken orally, once daily.

| | |
|---|---|
| **Arm title** | Group 2: BIC/FTC/TAF |

Arm description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF) |
| Investigational medicinal product code | |
| Other name | Bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg BIC, 200 mg FTC, and 25 mg TAF combined in a single tablet, taken orally once daily.

| **Number of subjects in period 1** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF |
|---|---|---|
| Started | 298 | 301 |
| Treated | 298 | 299 |
| Completed | 59 | 34 |
| Not completed | 239 | 267 |
| Adverse event, serious fatal | 3 | - |
| Physician decision | 11 | 7 |
| Consent withdrawn by subject | 35 | 34 |
| Unknown | 6 | 30 |
| Sponsor Decision | 168 | 179 |
| Lost to follow-up | 16 | 17 |

## Period 2

| | |
|---|---|
| Period 2 title | Extension Study (Week 144 to 168) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1: DOR/ISL |

Arm description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for

an additional 24 weeks, up to Week 168.

| | |
|---|---|
| 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:

100 mg DOR/0.75 mg ISL fixed dose combination (FDC) single tablet taken once daily by mouth.

| | |
|---|---|
| **Arm title** | Group 2: BIC/FTC/TAF |

Arm description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Bictegravir (BIC)/emtricitabine (FTC)/tenofovir alafenamide (TAF) |
| Investigational medicinal product code | |
| Other name | Bictegravir/emtricitabine/tenofovir alafenamide (BIC/FTC/TAF) |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg BIC, 200 mg FTC, and 25 mg TAF combined in a single tablet, taken orally once daily.

| **Number of subjects in period 2[1]** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF |
|---|---|---|
| Started | 21 | 27 |
| Completed | 0 | 1 |
| Not completed | 21 | 26 |
| Consent withdrawn by subject | 1 | - |
| Sponsor Decision | 20 | 25 |
| Lost to follow-up | - | 1 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subset of participants who completed the base study may have been eligible to enter the study extension. The extension was optional, and, in many cases, participants declined or chose to switch to another study.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Group 1: DOR/ISL |
| Reporting group description: | |
| Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168. | |
| Reporting group title | Group 2: BIC/FTC/TAF |
| Reporting group description: | |
| Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168. | |

| Reporting group values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | Total |
|---|---|---|---|
| Number of subjects | 298 | 301 | 599 |
| Age categorical<br>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) | 295 | 299 | 594 |
| From 65-84 years | 3 | 2 | 5 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: Years | | | |
| arithmetic mean | 34.7 | 35.7 | |
| standard deviation | ± 11.0 | ± 10.9 | - |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 77 | 71 | 148 |
| Male | 221 | 230 | 451 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 2 | 2 | 4 |
| Asian | 16 | 20 | 36 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 86 | 90 | 176 |
| White | 171 | 169 | 340 |
| More than one race | 23 | 19 | 42 |

| | | | |
|---|---|---|---|
| Unknown or Not Reported | 0 | 1 | 1 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 123 | 112 | 235 |
| Not Hispanic or Latino | 171 | 184 | 355 |
| Unknown or Not Reported | 4 | 5 | 9 |
| Baseline Human Immunodeficiency Virus (HIV)-1 Ribonucleic Acid (RNA) Level | | | |
| The Abbott RealTime polymerase chain reaction (PCR) assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. Participants were stratified into the following baseline HIV-1 RNA levels: ≤100,000 copies/mL, >100,000 copies/mL or missing. | | | |
| Units: Subjects | | | |
| ≤100,000 copies/mL | 244 | 239 | 483 |
| >100,000 copies/mL | 54 | 60 | 114 |
| Missing | 0 | 2 | 2 |
| Baseline Cluster of Differentiation 4+ (CD4+) T-Cell Count | | | |
| Plasma CD4+ T-cell count was measured in cells/mm^3 for baseline by a central laboratory. Baseline measurements were defined as the Day 1 value of each participant. Participants were stratified into the following baseline CD4+ T-cell counts: <200 cells/mm^3, ≥200 cells/mm^3, or missing. | | | |
| Units: Subjects | | | |
| <200 cells/mm^3 | 61 | 60 | 121 |
| ≥200 cells/mm^3 | 237 | 239 | 476 |
| Missing | 0 | 2 | 2 |

## End points

### End points reporting groups

| Reporting group title | Group 1: DOR/ISL |
|---|---|

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 2: BIC/FTC/TAF |
|---|---|

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 1: DOR/ISL |
|---|---|

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 2: BIC/FTC/TAF |
|---|---|

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

### 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:

The Abbott RealTime polymerase chain reaction (PCR) assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <50 copies/mL at Week 48 was presented using the Food and Drug Administration (FDA) Snapshot missing data approach. The analysis population consisted of all randomized participants who received at least one dose of study intervention. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Primary |
|---|---|

End point timeframe:

Week 48

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 88.9 | 88.3 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 2: BIC/FTC/TAF v Group 1: DOR/ISL |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| Parameter estimate | Treatment Difference |
| Point estimate | 0.46 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.73 |
| upper limit | 5.6 |

Notes:

[1] - Non-inferiority was concluded if the upper bound of the 2-sided multiplicity-adjusted 95% confidence interval (95%CI) was less than 10 percentage points. Estimated differences, CIs, & p-value for treatment differences in percent response were calculated using Miettinen & Nurminen method stratified by stratum with CMH weights; multiplicity-adjusted 95% CI corresponds to 1-sided Type 1 error of 0.02495

### Primary: Percentage of Participants Who Experienced an Adverse Event (AE) up to Week 48

| End point title | Percentage of Participants Who Experienced an Adverse Event (AE) up to Week 48 |
|---|---|

End point description:

An AE was any untoward medical occurrence in a study participant administered a study drug, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug whether or not it is considered related to the study drug. The percentage of participants who experienced at least one AE up to Week 48 was reported. The analysis population consisted of all randomized participants who received at least one dose of study intervention. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Primary |
|---|---|

End point timeframe:

Up to approximately 48 weeks

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 90.6 | 86.3 | | |

**Statistical analyses**

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | other[2] |
| Parameter estimate | Percentage Difference |
| Point estimate | 4.3 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.8 |
| upper limit | 9.6 |

Notes:

[2] - Difference between treatment groups (Group 1: DOR/ISL and Group 2: BIC/FTC/TAF). Miettinen & Nurminen method was used to generate percentage difference and the associated 95%CI.

**Primary: Percentage of Participants Who Discontinued Study Treatment Due to an AE up to Week 48**

| End point title | Percentage of Participants Who Discontinued Study Treatment Due to an AE up to Week 48 |
|---|---|

End point description:

An AE was any untoward medical occurrence in a study participant administered a study drug, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug whether or not it is considered related to the study drug. The percentage of participants who discontinued study treatment due to an AE up to Week 48 were reported. The analysis population consisted of all randomized participants who received at least one dose of study intervention. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Primary |
|---|---|

End point timeframe:

Up to approximately 48 weeks

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 7.4 | 3.3 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | other[3] |
| Parameter estimate | Percentage Difference |
| Point estimate | 4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.4 |
| upper limit | 7.9 |

Notes:

[3] - Difference between treatment groups (Group 1: DOR/ISL and Group 2: BIC/FTC/TAF). Miettinen & Nurminen method was used to generate percentage difference and the associated 95%CI.

### Secondary: Percentage of Participants with HIV-1 RNA <50 copies/mL at Week 96

| End point title | Percentage of Participants with HIV-1 RNA <50 copies/mL at Week 96 |
|---|---|

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <50 copies/mL at Week 96 was 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. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 96

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 51.7 | 57.9 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[4] |
| P-value | = 0.945 [5] |
| Method | Miettinen and Nurminen method |
| Parameter estimate | Estimated Difference |
| Point estimate | -6.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.21 |
| upper limit | 1.46 |

Notes:

[4] - Non-inferiority was concluded if the upper bound of the 2-sided multiplicity-adjusted 95% confidence interval (95%CI) was less than 10 percentage points. The multiplicity-adjusted 95% CI is shown corresponding to a 1-sided Type 1 error of 0.02495. Estimated Difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

[5] - The estimated differences, CIs and p-value for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights.

## Secondary: Percentage of Participants with HIV-1 RNA <50 copies/mL at Week 144

| End point title | Percentage of Participants with HIV-1 RNA <50 copies/mL at Week 144 |
|---|---|

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <50 copies/mL at Week 144 was presented using the Data as Observed (DAO) missing data approach. 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 at Week 144. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 41 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 64.1 | 82.9 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |

| | |
|---|---|
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other[6] |
| Parameter estimate | Estimated Difference |
| Point estimate | -19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38 |
| upper limit | 0.2 |

Notes:

[6] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights. Estimated Difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

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

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

End point description:

The percentage of participants with HIV-1 RNA <40 copies/mL was determined. The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <40 copies/mL at Week 48 was 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. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Week 48

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 88.6 | 86.3 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[7] |
| Parameter estimate | Treatment Difference |
| Point estimate | 2.12 |

| | |
|---|---|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.23 |
| upper limit | 7.48 |

Notes:

[7] - Non-inferiority was concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI was less than 10 percentage points. The estimated differences, CIs and p-value for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights.

## Secondary: Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 48

| | |
|---|---|
| End point title | Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 48 |

End point description:

The percentage of participants with HIV-1 RNA <200 copies/mL was determined. The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <200 copies/mL at Week 48 was 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. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| | |
|---|---|
| End point type | Secondary |

End point timeframe:

Week 48

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 89.6 | 88.6 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[8] |
| Parameter estimate | Treatment Difference |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.25 |
| upper limit | 5.9 |

Notes:

[8] - Non-inferiority was concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI was less than 10 percentage points. The estimated differences, CIs and p-value for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with

Cochran-Mantel-Haenszel (CMH) weights.

| Secondary: Percentage of Participants with HIV-1 RNA <40 copies/mL at Week 96 | |
|---|---|
| End point title | Percentage of Participants with HIV-1 RNA <40 copies/mL at Week 96 |

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <40 copies/mL at Week 96 was 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. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 96

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 51.0 | 57.5 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | other[9] |
| Parameter estimate | Estimated Difference |
| Point estimate | -6.74 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.53 |
| upper limit | 1.15 |

Notes:

[9] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The estimated differences, and confidence intervals (CIs) for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights. Estimated difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

| Secondary: Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 96 | |
|---|---|
| End point title | Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 96 |

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <200 copies/mL at Week 96 was 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. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 96

| **End point values** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 52.3 | 58.5 | | |

**Statistical analyses**

| **Statistical analysis title** | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 597 |
| Analysis specification | Pre-specified |
| Analysis type | other[10] |
| Parameter estimate | Estimated Difference |
| Point estimate | -6.41 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -14.2 |
| upper limit | 1.46 |

Notes:

[10] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The estimated differences, and confidence intervals (CIs) for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights. Estimated difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

## Secondary: Percentage of Participants with HIV-1 RNA <40 copies/mL at Week 144

| End point title | Percentage of Participants with HIV-1 RNA <40 copies/mL at Week 144 |
|---|---|

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <40 copies/mL at Week 144 was presented using the DAO missing data approach. 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 at Week 144. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 41 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 64.1 | 82.9 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other[11] |
| Parameter estimate | Estimated Difference |
| Point estimate | -19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38 |
| upper limit | 0.2 |

Notes:

[11] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights. Estimated difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

### Secondary: Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 144

| End point title | Percentage of Participants with HIV-1 RNA <200 copies/mL at Week 144 |
|---|---|

End point description:

The Abbott RealTime PCR assay with a reliable lower limit of quantification of 40 copies/mL was used to measure the HIV-1 RNA level in blood samples obtained at each visit. The percentage of participants with HIV-1 RNA <200 copies/mL at Week 144 was presented using the DAO missing data approach. 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 at Week 144. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 39 | 41 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 64.1 | 82.9 | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 80 |
| Analysis specification | Pre-specified |
| Analysis type | other[12] |
| Parameter estimate | Estimated Difference |
| Point estimate | -19.5 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38 |
| upper limit | 0.2 |

Notes:

[12] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for the treatment differences in percent response were calculated using the Miettinen and Nurminen method stratified by stratum with Cochran-Mantel-Haenszel (CMH) weights. Estimated difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

### Secondary: Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 48

| End point title | Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 48 |
|---|---|

End point description:

Plasma CD4+ T-cell count was measured in cells/mm^3 for baseline and at Week 48 by a central laboratory. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in CD4+ T-cell count at Week 48 using the Data as Observed (DAO) approach was presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available, including baseline data available for CD4+ T-cell count at Week 48. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 48

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 263 | 263 | | |
| Units: cells/mm^3 | | | | |
| arithmetic mean (confidence interval 95%) | 182.4 (162.0 to 202.7) | 233.5 (211.8 to 255.3) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 96

| End point title | Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 96 |
|---|---|

End point description:

Plasma CD4+ T-cell count was measured in cells/mm^3 for baseline and at Week 96 by a central laboratory. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in CD4+ T-cell count at Week 96 using the Data as Observed (DAO) approach was presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available, including baseline data available for CD4+ T-cell count at Week 96. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 96

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 159 | 168 | | |
| Units: cells/mm^3 | | | | |
| arithmetic mean (confidence interval 95%) | 217.05 (187.52 to 246.58) | 319.92 (290.53 to 349.32) | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 327 |
| Analysis specification | Pre-specified |
| Analysis type | other[13] |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -91.75 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -132.59 |
| upper limit | -50.9 |

Notes:

[13] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for mean difference in CD4+ T-cell count change from baseline were based on analysis of covariance (ANCOVA) models adjusted by baseline CD4+ T-cell count, stratum, and treatment group. Mean difference is Treatment difference for DOR/ISL group minus BIC/FTC/TAF group.

## Secondary: Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 144

| End point title | Mean Change from Baseline in Cluster of Differentiation 4+ (CD4+) T-Cell Counts at Week 144 |
|---|---|

End point description:

Plasma CD4+ T-cell count was measured in cells/mm^3 for baseline and at Week 144 by a central laboratory. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in CD4+ T-cell count at Week 144 using the Data as Observed (DAO) approach was presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available, including baseline data available for CD4+ T-cell count at Week 144. Participants were included in the treatment group to which they were randomized. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 32 | | |
| Units: cells/mm^3 | | | | |
| arithmetic mean (confidence interval 95%) | 239.6 (177.4 to 301.8) | 350.9 (265.7 to 436.1) | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 56 |
| Analysis specification | Pre-specified |
| Analysis type | other[14] |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -111.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -218.8 |
| upper limit | -4.8 |

Notes:

[14] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for mean difference in CD4+ T-cell count change from baseline were based on analysis of covariance (ANCOVA) models adjusted by baseline CD4+ T-cell count, stratum, and treatment group. Mean Difference is Treatment Difference (DOR/ISL minus BIC/FTC/TAF) .

## Secondary: Incidence of Viral Resistance-Associated Substitutions (RASs) at Week 48

| End point title | Incidence of Viral Resistance-Associated Substitutions (RASs) at Week 48 |
|---|---|

End point description:

RASs was defined as participants with confirmed HIV-1 RNA ≥200 copies/mL and/or genotypic or phenotypic analysis of data showing evidence of resistance to the study drug administered. The number of participants who demonstrated RASs at Week 48 was presented. The analysis population consisted of participants with data available at Week 48. Per protocol, participants who met the definition of confirmed virologic rebound or incomplete virologic response, or who discontinued study intervention for another reason and had HIV-1 RNA ≥200 copies/mL at the time of discontinuation. Among such participants, those with HIV-1 RNA ≥400 copies/mL were included. Participants for whom available genotypic or phenotypic data showed evidence of resistance, irrespective of viral load, were also included. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 48

| **End point values** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 6 | | |
| Units: Participants | 1 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of Viral RASs at Week 96

| End point title | Incidence of Viral RASs at Week 96 |
|---|---|

End point description:

RASs was defined as participants with confirmed HIV-1 RNA ≥200 copies/mL and/or genotypic or phenotypic analysis of data showing evidence of resistance to the study drug administered. The number of participants who demonstrated RASs at Week 96 was presented. The analysis population consisted of participants with data available at Week 96. Per protocol, participants who met the definition of confirmed virologic rebound or incomplete virologic response, or who discontinued study intervention for another reason and had HIV-1 RNA ≥200 copies/mL at the time of discontinuation. Among such participants, those with HIV-1 RNA ≥400 copies/mL were included. Participants for whom available genotypic or phenotypic data showed evidence of resistance, irrespective of viral load, were also included. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 96

| **End point values** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 9 | | |
| Units: Participants | 2 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Incidence of Viral RASs at Week 144

| End point title | Incidence of Viral RASs at Week 144 |
|---|---|

End point description:

RASs was defined as participants with confirmed HIV-1 RNA ≥200 copies/mL and/or genotypic or phenotypic analysis of data showing evidence of resistance to the study drug administered. The number of participants who demonstrated RASs at Week 144 was presented. The analysis population consisted of participants with data available at Week 144. Per protocol, participants who met the definition of confirmed virologic rebound or incomplete virologic response, or who discontinued study intervention for another reason and had HIV-1 RNA ≥200 copies/mL at the time of discontinuation. Among such participants, those with HIV-1 RNA ≥400 copies/mL were included. Participants for whom available genotypic or phenotypic data showed evidence of resistance, irrespective of viral load, were also included. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5 | 9 | | |
| Units: Participants | 2 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change From Baseline in Body Weight at Week 96

| End point title | Mean Change From Baseline in Body Weight at Week 96 |
|---|---|

End point description:

Body weight was measured at baseline and at Week 96. Participants removed their shoes and wore a single layer of clothing at each measurement. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in body weight at Week 96 was presented. The analysis population consisted of all randomized participants who received at least one dose of intervention and had data available, including baseline data available, for this outcome measure at Week 96. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 96

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 189 | 201 | | |
| Units: kilogram | | | | |
| arithmetic mean (confidence interval 95%) | 3.31 (2.45 to 4.18) | 4.13 (3.15 to 5.11) | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 390 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[15] |
| P-value | = 0.268 [16] |
| Method | ANCOVA |
| Parameter estimate | Estimated Difference |
| Point estimate | -0.74 |
| Confidence interval | |
| level | Other: 97 % |
| sides | 2-sided |
| lower limit | -2.19 |
| upper limit | 0.71 |

Notes:

[15] - Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI was less than 0. The CIs for treatment difference were calculated from ANCOVA models with terms for baseline weight, sex, race, stratum & treatment. A 2-sided p-value was calculated using ANCOVA model. The CIs at week 96 is 97% corresponds to a 1-sided Type 1 error of 0.015.

[16] - A 2-sided p-value was calculated using the Analysis of covariance (ANCOVA) model.

### Secondary: Mean Change From Baseline in Body Weight at Week 48

| End point title | Mean Change From Baseline in Body Weight at Week 48 |
|---|---|

End point description:

Body weight was measured at baseline and at Week 48. Participants removed their shoes and wore a single layer of clothing at each measurement. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in body weight at Week 48 was presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available, including baseline data available, for this outcome measure at Week 48. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 48

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 270 | 268 | | |
| Units: kilogram | | | | |
| arithmetic mean (confidence interval 95%) | 3.45 (2.83 to 4.06) | 3.32 (2.68 to 3.96) | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 538 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[17] |
| P-value | = 0.73 [18] |
| Method | ANCOVA |
| Parameter estimate | Treatment Difference |
| Point estimate | 0.15 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.71 |
| upper limit | 1.02 |

Notes:

[17] - Superiority will be concluded if the upper bound of the 2-sided multiplicity-adjusted 95% CI was less than 0. A 2-sided p-value was calculated using the Analysis of covariance (ANCOVA) model. ANCOVA model was used to generate treatment difference and the associated 95%CI.
[18] - A 2-sided p-value was calculated using the Analysis of covariance (ANCOVA) model.

## Secondary: Percentage of Participants Who Experienced an Adverse Event (AE)

| End point title | Percentage of Participants Who Experienced an Adverse Event (AE) |
|---|---|

End point description:

An AE was any untoward medical occurrence in a study participant administered a study drug, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug whether or not it is considered related to the study drug. The percentage of participants who experienced at least one or more AEs is presented. Per protocol, pregnancy-related AEs collected for enrolled participants are reported separately and are presented in the AE module. The analysis population consisted of all randomized participants who received at least one dose of study intervention. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to approximately 47 months

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 96.6 | 94.0 | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Mean Change From Baseline in Body Weight at Week 144

| End point title | Mean Change From Baseline in Body Weight at Week 144 |
|---|---|

End point description:

Body weight was measured at baseline and at Week 144. Participants removed their shoes and wore a single layer of clothing at each measurement. Baseline measurements were defined as the Day 1 value of each participant. The mean change from baseline in body weight at Week 144 was presented. The analysis population consisted of all randomized participants who received at least one dose of study intervention and had data available, including baseline data available, for this outcome measure at Week 144. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Baseline (Day 1) and Week 144

| End point values | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 40 | 42 | | |
| Units: kilogram | | | | |
| arithmetic mean (confidence interval 95%) | 4.55 (2.40 to 6.70) | 3.55 (-1.46 to 8.56) | | |

### Statistical analyses

| Statistical analysis title | Difference between treatment groups |
|---|---|
| Comparison groups | Group 1: DOR/ISL v Group 2: BIC/FTC/TAF |
| Number of subjects included in analysis | 82 |
| Analysis specification | Pre-specified |
| Analysis type | other[19] |
| Parameter estimate | Estimated Difference |
| Point estimate | 1.08 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.07 |
| upper limit | 6.24 |

Notes:

[19] - Type of statistical test 'other' denotes no hypothesis testing was conducted. The CIs for treatment difference were calculated from the Analysis of covariance (ANCOVA) models with terms for baseline weight, sex, race, stratum and treatment.

## Secondary: Percentage of Participants Who Discontinued Study Treatment Due to an AE

| End point title | Percentage of Participants Who Discontinued Study Treatment Due to an AE |
|---|---|

End point description:

An AE was any untoward medical occurrence in a study participant administered a study drug, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug whether or not it is considered related to the study drug. The percentage of participants who discontinued study intervention due to an AE is presented. Per protocol, pregnancy-related AEs collected for enrolled participants are reported separately and are presented in the AE module. The analysis population consisted of all randomized participants who received at least one dose of study intervention. Participants were included in the treatment group corresponding to the study intervention received. The final analysis for this outcome is presented here.

| End point type | Secondary |
|---|---|

End point timeframe:

Up to approximately 38 months

| **End point values** | Group 1: DOR/ISL | Group 2: BIC/FTC/TAF | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 299 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 14.1 | 9.0 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to approximately 47 months

Adverse event reporting additional description:

All cause mortality: all randomized participants; AEs: all randomized participants who got ≥1 dose of study drug. Reported by base & extension. Per protocol, participants with drops in CD4+/total lymphocyte count reported as 'post treatment follow up'; all pregnancy-related AEs & infant SAEs collected & reported by arm that participants enrolled.

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 27.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Group 1: DOR/ISL Base Study Week 48-Week 96 |

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Reporting group title | Group 1: DOR/ISL Base Study Week 0 - Week 48 |

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Reporting group title | Group 2: BIC/FTC/TAF Open-Label Extension Week 144 - Week 168 |

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Reporting group title | Group 1: DOR/ISL Post-Treatment Follow-Up |

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| | |
|---|---|
| Reporting group title | Group 2: BIC/FTC/TAF Base Study Week 0 - Week 48 |

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 2: BIC/FTC/TAF Base Study Week 48 - Week 96 |
|---|---|

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 2: BIC/FTC/TAF Base Study Week 96 - Week 144 |
|---|---|

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 1: DOR/ISL Base Study Week 96-Week 144 |
|---|---|

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 2: BIC/FTC/TAF Post-Treatment Follow-Up |
|---|---|

Reporting group description:

Treatment-naïve participants living with HIV-1 that had not received ≤10 days of prior antiretroviral therapy received blinded BIC/FTC/TAF (50 mg bictegravir [BIC], 200 mg emtricitabine [FTC], 25 mg tenofovir alafenamide [TAF]) and placebo to FDC DOR/ISL QD from Day 1 to Week 96, and open-label BIC/FTC/TAF up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive QD BIC/FTC/TAF (50 mg/200 mg/25 mg) for an additional 24 weeks, up to Week 168.

| Reporting group title | Group 1: DOR/ISL Open-Label Extension Week 144-Week 168 |
|---|---|

Reporting group description:

Treatment-naïve participants living with human immunodeficiency virus-1 (HIV-1) that had not received ≤10 days of prior antiretroviral therapy received blinded fixed dose combination (FDC) Doravirine/Islatravir (DOR/ISL) (100 mg doravirine [DOR]/0.75 mg islatravir [ISL]) and placebo to Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/FTC/TAF) once daily (QD) from Day 1 to Week 96, and open-label DOR/ISL up to Week 144. At Week 144, participants who consent to enter the optional open-label study extension continued to receive open-label QD FDC of DOR/ISL (100 mg/0.75 mg) for an additional 24 weeks, up to Week 168.

| **Serious adverse events** | Group 1: DOR/ISL Base Study Week 48-Week 96 | Group 1: DOR/ISL Base Study Week 0 - Week 48 | Group 2: BIC/FTC/TAF Open-Label Extension Week 144 - Week 168 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 14 / 266 (5.26%) | 19 / 298 (6.38%) | 0 / 27 (0.00%) |
| number of deaths (all causes) | 0 | 2 | 0 |
| number of deaths resulting from adverse events | 0 | 2 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Diffuse large B-cell lymphoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 | | | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Abortion incomplete | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |

| | | | |
|---|---|---|---|
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 3 / 298 (1.01%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 | | | |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Depression | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Major depression | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal behaviour | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Suicide attempt | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 266 (0.38%) | 1 / 298 (0.34%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Craniofacial fracture | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |

| | | | |
|---|---|---|---|
| Suture rupture | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Stab wound | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Exomphalos | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Heart failure with preserved ejection fraction | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Pericarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |

| | | | |
|---|---|---|---|
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Acute hepatitis B | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 2 / 298 (0.67%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Cytomegalovirus colitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Lymphogranuloma venereum | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Neurosyphilis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Scrotal abscess | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Scrotal cellulitis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 266 (0.00%) | 0 / 298 (0.00%) | 0 / 27 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 266 (0.38%) | 0 / 298 (0.00%) | 0 / 27 (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 | | | |
| Diabetes mellitus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 266 (0.00%) | 1 / 298 (0.34%) | 0 / 27 (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 |

| **Serious adverse events** | Group 1: DOR/ISL Post-Treatment Follow-Up | Group 2: BIC/FTC/TAF Base Study Week 0 - Week 48 | Group 2: BIC/FTC/TAF Base Study Week 48 - Week 96 |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 112 (2.68%) | 16 / 299 (5.35%) | 13 / 267 (4.87%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from adverse events | 1 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Vascular disorders | | | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 incomplete | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Major depression | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Suicidal behaviour | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 | | | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Craniofacial fracture | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |

| | | | |
|---|---|---|---|
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suture rupture | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Stab wound | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Exomphalos | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Heart failure with preserved ejection fraction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Intestinal obstruction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute hepatitis B | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 2 / 299 (0.67%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Cytomegalovirus colitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Diverticulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Lymphogranuloma venereum | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Neurosyphilis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumocystis jirovecii pneumonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 1 / 267 (0.37%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scrotal abscess | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Scrotal cellulitis | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 0 / 267 (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 |
| Sepsis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (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 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 0 / 299 (0.00%) | 0 / 267 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Group 2: BIC/FTC/TAF Base Study Week 96 - Week 144 | Group 1: DOR/ISL Base Study Week 96-Week 144 | Group 2: BIC/FTC/TAF Post-Treatment Follow-Up |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 143 (0.70%) | 3 / 146 (2.05%) | 1 / 128 (0.78%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Hodgkin's disease | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Vascular disorders | | | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Deep vein thrombosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 incomplete | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 1 / 128 (0.78%) |
| 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 | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Anxiety disorder | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Depression | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Major depression | | | |
| subjects affected / exposed | 1 / 143 (0.70%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Suicidal behaviour | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 1 / 146 (0.68%) | 0 / 128 (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 |
| Craniofacial fracture | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Gun shot wound | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Poisoning | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Suture rupture | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Stab wound | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Exomphalos | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Heart failure with preserved ejection fraction | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 1 / 128 (0.78%) |
| 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 | | | |
| Abdominal pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Hepatitis acute | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 | | | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Abdominal wall abscess | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Acute hepatitis B | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Bacterial infection | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Cytomegalovirus colitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Disseminated tuberculosis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Diverticulitis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 1 / 146 (0.68%) | 0 / 128 (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 |
| Infectious pleural effusion | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Lymphogranuloma venereum | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Neurosyphilis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Peritonitis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia pneumococcal | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Scrotal abscess | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 1 / 146 (0.68%) | 0 / 128 (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 |
| Scrotal cellulitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 143 (0.00%) | 1 / 146 (0.68%) | 0 / 128 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 1 / 146 (0.68%) | 0 / 128 (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 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (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 |
| Metabolism and nutrition disorders | | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Group 1: DOR/ISL Open-Label Extension Week 144-Week 168 | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Diffuse large B-cell lymphoma | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hodgkin's disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abortion incomplete | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gestational hypertension | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Anxiety disorder | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Major depression | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal behaviour | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicide attempt | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Liver function test increased | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| Ankle fracture | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Craniofacial fracture | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hand fracture | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gun shot wound | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Poisoning | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Suture rupture | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Stab wound | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Exomphalos | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angina unstable | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Heart failure with preserved ejection fraction | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericarditis | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Migraine | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile convulsion | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophagitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| Cholelithiasis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatitis acute | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |

| | | | | |
|---|---|---|---|---|
| Acute kidney injury | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal and connective tissue disorders | | | | |
| Intervertebral disc protrusion | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Abdominal wall abscess | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abscess limb | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Acute hepatitis B | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COVID-19 | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacterial infection | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| Cellulitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COVID-19 pneumonia | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cytomegalovirus colitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disseminated tuberculosis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diverticulitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious pleural effusion | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lymphogranuloma venereum | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neurosyphilis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumocystis jirovecii pneumonia | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peritonsillar abscess | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia bacterial | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia pneumococcal | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary tuberculosis | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Scrotal abscess | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Scrotal cellulitis | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Septic shock | | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 21 (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 / 21 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders | | | | |
| Diabetes mellitus | | | | |
| subjects affected / exposed | 0 / 21 (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 Base Study Week 48-Week 96 | Group 1: DOR/ISL Base Study Week 0 - Week 48 | Group 2: BIC/FTC/TAF Open-Label Extension Week 144 - Week 168 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 115 / 266 (43.23%) | 146 / 298 (48.99%) | 2 / 27 (7.41%) |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 28 / 266 (10.53%) | 2 / 298 (0.67%) | 1 / 27 (3.70%) |
| occurrences (all) | 35 | 2 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 2 / 266 (0.75%) | 19 / 298 (6.38%) | 1 / 27 (3.70%) |
| occurrences (all) | 2 | 19 | 1 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 64 / 266 (24.06%) | 27 / 298 (9.06%) | 0 / 27 (0.00%) |
| occurrences (all) | 75 | 28 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 7 / 266 (2.63%) | 17 / 298 (5.70%) | 0 / 27 (0.00%) |
| occurrences (all) | 12 | 21 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 13 / 266 (4.89%) | 31 / 298 (10.40%) | 0 / 27 (0.00%) |
| occurrences (all) | 14 | 36 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 266 (2.26%) | 26 / 298 (8.72%) | 0 / 27 (0.00%) |
| occurrences (all) | 7 | 28 | 0 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 4 / 266 (1.50%) | 13 / 298 (4.36%) | 0 / 27 (0.00%) |
| occurrences (all) | 4 | 14 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 11 / 266 (4.14%) | 16 / 298 (5.37%) | 0 / 27 (0.00%) |
| occurrences (all) | 12 | 17 | 0 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| COVID-19 | | | |
| subjects affected / exposed | 20 / 266 (7.52%) | 42 / 298 (14.09%) | 1 / 27 (3.70%) |
| occurrences (all) | 21 | 45 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 14 / 266 (5.26%) | 15 / 298 (5.03%) | 0 / 27 (0.00%) |
| occurrences (all) | 14 | 16 | 0 |

| **Non-serious adverse events** | Group 1: DOR/ISL Post-Treatment Follow-Up | Group 2: BIC/FTC/TAF Base Study Week 0 - Week 48 | Group 2: BIC/FTC/TAF Base Study Week 48 - Week 96 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 112 (7.14%) | 141 / 299 (47.16%) | 124 / 267 (46.44%) |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 1 / 299 (0.33%) | 25 / 267 (9.36%) |
| occurrences (all) | 0 | 1 | 28 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 18 / 299 (6.02%) | 8 / 267 (3.00%) |
| occurrences (all) | 1 | 18 | 8 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 12 / 299 (4.01%) | 55 / 267 (20.60%) |
| occurrences (all) | 0 | 12 | 62 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 16 / 299 (5.35%) | 17 / 267 (6.37%) |
| occurrences (all) | 0 | 24 | 24 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 112 (0.89%) | 34 / 299 (11.37%) | 13 / 267 (4.87%) |
| occurrences (all) | 1 | 38 | 15 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 20 / 299 (6.69%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 21 | 5 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 112 (1.79%) | 19 / 299 (6.35%) | 3 / 267 (1.12%) |
| occurrences (all) | 2 | 20 | 3 |

| | | | |
|---|---|---|---|
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 14 / 299 (4.68%) | 5 / 267 (1.87%) |
| occurrences (all) | 0 | 16 | 6 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 0 / 112 (0.00%) | 47 / 299 (15.72%) | 29 / 267 (10.86%) |
| occurrences (all) | 0 | 49 | 29 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 112 (6.25%) | 15 / 299 (5.02%) | 11 / 267 (4.12%) |
| occurrences (all) | 8 | 18 | 11 |

| **Non-serious adverse events** | Group 2: BIC/FTC/TAF Base Study Week 96 - Week 144 | Group 1: DOR/ISL Base Study Week 96-Week 144 | Group 2: BIC/FTC/TAF Post-Treatment Follow-Up |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 37 / 143 (25.87%) | 42 / 146 (28.77%) | 2 / 128 (1.56%) |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 14 / 143 (9.79%) | 12 / 146 (8.22%) | 0 / 128 (0.00%) |
| occurrences (all) | 17 | 13 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 1 / 143 (0.70%) | 0 / 146 (0.00%) | 0 / 128 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 24 / 143 (16.78%) | 25 / 146 (17.12%) | 0 / 128 (0.00%) |
| occurrences (all) | 27 | 29 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 143 (0.70%) | 3 / 146 (2.05%) | 0 / 128 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 143 (1.40%) | 2 / 146 (1.37%) | 0 / 128 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 143 (1.40%) | 2 / 146 (1.37%) | 1 / 128 (0.78%) |
| occurrences (all) | 2 | 2 | 1 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 143 (0.70%) | 1 / 146 (0.68%) | 0 / 128 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 143 (0.00%) | 2 / 146 (1.37%) | 0 / 128 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Infections and infestations | | | |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 143 (2.10%) | 2 / 146 (1.37%) | 1 / 128 (0.78%) |
| occurrences (all) | 3 | 2 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 143 (2.80%) | 4 / 146 (2.74%) | 0 / 128 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |

| **Non-serious adverse events** | Group 1: DOR/ISL Open-Label Extension Week 144-Week 168 | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| Investigations | | | |
| CD4 lymphocytes decreased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight increased | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 0 / 21 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Headache<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | | |
| Gastrointestinal disorders<br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | | |
| Psychiatric disorders<br>Insomnia<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | | |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0 | | |
| Infections and infestations<br>COVID-19<br>subjects affected / exposed<br>occurrences (all)<br>Upper respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 0 / 21 (0.00%)<br>0<br>0 / 21 (0.00%)<br>0 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 08 June 2020 | Amendment 01: The protocol was amended to: (1) update the hypothesis testing strategy in the statistical analysis plan, (2) update the prohibited concomitant therapies, and (3) allow participants to rescreen one time following approval from the Sponsor. |
| 30 June 2021 | Amendment 02: The protocol was amended to: (1) extend study intervention (open-label) from 96 weeks to 144 weeks for all participants; (2) provide an option for Group 2 to receive open-label DOR/ISL from Week 144 to Week 156; (3) offer the option to continue study intervention for participants who become pregnant; and (4) add a discontinuation criterion if a participant chooses to breastfeed. |
| 22 February 2022 | Amendment 04: The protocol was amended to: (1) 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, given the findings of decreases in CD4+ T-cell and total lymphocyte counts in clinical studies evaluating ISL and (2) to update the timing of when the Sponsor will be unblinded to individual participants' treatment assignments. |
| 04 December 2022 | Amendment 05: This protocol was amended to allow participants who continue to benefit (as determined by the Investigator) from their assigned study intervention, to continue their assigned study intervention through a study extension after Week 144. This extension will continue for up to 24 additional weeks (up to maximum Week 168) or until the participant has the option to enroll in a DOR/ISL 100 mg/0.25 mg study; whichever is sooner. Participants choosing not to enroll in a DOR/ISL 100 mg/0.25 mg study, will transition to commercially available ART as soon as possible. |
| 20 May 2024 | Amendment 06: 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