



Clinical trial results:

Phase IIb, Double-Blinded, Multicenter, Randomized Study to Assess the Effect on Central Nervous System (CNS) Toxicity of Switching from ATRIPLA™ (Efavirenz, Tenofovir, Emtricitabine) to MK-1439A (Doravirine, Tenofovir, Lamivudine) in Virologically-Suppressed Subjects

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-003617-18 |
| Trial protocol | GB IE |
| Global end of trial date | 07 February 2024 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 09 February 2025 |
| First version publication date | 09 February 2025 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | MK-1439A-028 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02652260 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Merck Sharp & Dohme LLC |
| Sponsor organisation address | 126 East Lincoln Avenue, P.O. Box 2000, Rahway, NJ, United States, 07065 |
| Public contact | Clinical Trials Disclosure, Merck Sharp & Dohme LLC, ClinicalTrialsDisclosure@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 | 07 February 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 August 2018 |
| Global end of trial reached? | Yes |
| Global end of trial date | 07 February 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This study aims to evaluate a switch from fixed dose combination (FDC) treatment with ATRIPLATM for 12 weeks prior to screening to FDC treatment with Doravirine, Tenofovir, Lamivudine (MK-1439A) in virologically-suppressed, human immunodeficiency virus type 1 (HIV-1)-infected participants. The primary hypothesis is that switching from ATRIPLATM to Doravirine, Tenofovir, Lamivudine results in a lower proportion of participants with at least one CNS toxicity of at least Grade 2 intensity at Week 12 than continuation of ATRIPLATM treatment.

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 | 04 March 2016 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Ireland: 2 |
| Country: Number of subjects enrolled | South Africa: 45 |
| Country: Number of subjects enrolled | United Kingdom: 39 |
| Worldwide total number of subjects | 86 |
| EEA total number of subjects | 2 |

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) | 82 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Out of 112 participants screened, 86 were randomized and received study treatment.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|------------------------------|
| Arm title | Immediate Switch to MK-1439A |
|------------------|------------------------------|

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

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

Dosage and administration details:

A single tablet FDC containing doravirine 100 mg, lamivudine (3TC) 300 mg and tenofovir disoproxil fumarate (TDF) 300 mg administered orally, once daily for 12 weeks during the Blinded period and 12 weeks during the Open-Label period.

| | |
|--|---------------------|
| Investigational medicinal product name | Placebo to ATRIPLA™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single placebo to ATRIPLA™ tablet administered orally, once daily for 12 weeks during the Blinded period.

| | |
|--|--|
| Investigational medicinal product name | Placebo to Doravirine, Tenofovir, Lamivudine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single placebo to doravirine, tenofovir, lamivudine tablet administered orally, once daily for 12 weeks during the Blinded period.

| | |
|------------------|-----------------------------|
| Arm title | Deferred Switch to MK-1439A |
|------------------|-----------------------------|

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week

12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | ATRIPLA™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single tablet FDC containing efavirenz (EFV) 600 mg, emtricitabine (FTC) 200 mg, and TDF 300 mg administered orally, once daily for 12 weeks during the Blinded period.

| | |
|--|-----------------------------------|
| Investigational medicinal product name | Doravirine, Tenofovir, Lamivudine |
| Investigational medicinal product code | |
| Other name | MK-1439A |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for 24 weeks during the Open-Label period.

| Number of subjects in period 1 | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A |
|--------------------------------|------------------------------|-----------------------------|
| Started | 43 | 43 |
| Switched Over to MK-1439A | 0 ^[1] | 42 |
| Completed | 43 | 41 |
| Not completed | 0 | 2 |
| Consent withdrawn by subject | - | 1 |
| Pregnancy | - | 1 |

Notes:

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

Justification: Only participants in the Deferred Switch to MK-1439A arm switched treatments.

Period 2

| | |
|------------------------------|--------------------------------|
| Period 2 title | Study Extension 1 (Open-Label) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Immediate Switch to MK-1439A |

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

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

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for an additional 96 weeks during the Open-Label extension period 1.

| | |
|------------------|-----------------------------|
| Arm title | Deferred Switch to MK-1439A |
|------------------|-----------------------------|

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

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

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for an additional 96 weeks during the Open-Label extension period 1.

| Number of subjects in period 2 | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A |
|---------------------------------------|------------------------------|-----------------------------|
| Started | 43 | 41 |
| Completed | 39 | 34 |
| Not completed | 4 | 7 |
| Consent withdrawn by subject | 1 | 2 |
| Availability of study drug locally | 1 | 1 |
| Adverse event, non-fatal | - | 2 |
| Pregnancy | 1 | 1 |
| Lack of efficacy | 1 | 1 |

Period 3

| | |
|------------------------------|--------------------------------|
| Period 3 title | Study Extension 2 (Open-Label) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|--|-----------------------------------|
| Arm title | Immediate Switch to MK-1439A |
| Arm description: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Arm type | Experimental |
| Investigational medicinal product name | Doravirine, Tenofovir, Lamivudine |
| Investigational medicinal product code | |
| Other name | MK-1439A |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 228 weeks during the Open-Label extension period 2.

| | |
|---|-----------------------------------|
| Arm title | Deferred Switch to MK-1439A |
| Arm description: Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |
| Arm type | Active comparator |
| Investigational medicinal product name | Doravirine, Tenofovir, Lamivudine |
| Investigational medicinal product code | |
| Other name | MK-1439A |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 228 weeks during the Open-Label extension period 2.

| Number of subjects in period 3^[2] | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A |
|---|------------------------------|-----------------------------|
| Started | 39 | 33 |
| Completed | 17 | 19 |
| Not completed | 22 | 14 |
| Adverse event, non-fatal | 1 | - |
| Availability of study drug locally | 18 | 13 |
| Pregnancy | 1 | 1 |
| Non-Compliance with study drug | 1 | - |
| Lost to follow-up | 1 | - |

Notes:

[2] - 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.

Period 4

| | |
|------------------------------|--------------------------------|
| Period 4 title | Study Extension 3 (Open-Label) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Immediate Switch to MK-1439A |

Arm description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312).

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

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 324 weeks during the Open-Label extension period 3.

| | |
|------------------|-----------------------------|
| Arm title | Deferred Switch to MK-1439A |
|------------------|-----------------------------|

Arm description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324).

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

Dosage and administration details:

A single-tablet FDC containing doravirine 100 mg, 3TC 300 mg and TDF 300 mg administered orally, once daily for a maximum total duration of treatment of 324 weeks during the Open-Label extension period 3

| Number of subjects in period 4 | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A |
|---------------------------------------|------------------------------|-----------------------------|
| Started | 17 | 19 |
| Completed | 10 | 8 |
| Not completed | 7 | 11 |
| Physician decision | 7 | 10 |
| Pregnancy | - | 1 |

Baseline characteristics

Reporting groups

| | |
|--|------------------------------|
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |

| Reporting group values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | Total |
|--|------------------------------|-----------------------------|-------|
| Number of subjects | 43 | 43 | 86 |
| Age categorical | | | |
| Units: Participants | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 40 | 42 | 82 |
| From 65-84 years | 3 | 1 | 4 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 41.8 | 41.6 | |
| standard deviation | ± 11.9 | ± 11.2 | - |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 19 | 17 | 36 |
| Male | 24 | 26 | 50 |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 3 | 1 | 4 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 25 | 23 | 48 |
| White | 12 | 19 | 31 |
| More than one race | 3 | 0 | 3 |
| Unknown or Not Reported | 0 | 0 | 0 |
| Ethnicity (NIH/OMB) | | | |

| | | | |
|--|---------|---------|----|
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 1 | 5 |
| Not Hispanic or Latino | 39 | 42 | 81 |
| Unknown or Not Reported | 0 | 0 | 0 |
| CNS Toxicity Percentage Of Maximum Score | | | |
| Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing across all 10 CNS toxicities and converting the sum to a percentage of the maximum possible sum of intensities (10 x 3 = 30). A higher CNS score indicates worsening symptoms. | | | |
| Units: Percentage of maximum score | | | |
| arithmetic mean | 32.9 | 37.1 | |
| standard deviation | ± 16.5 | ± 19.0 | - |
| Fasting Lipids - LDL Cholesterol | | | |
| Mean concentrations of low-density lipoprotein (LDL) cholesterol. All randomized participants who received at least one dose of study treatment were analyzed. | | | |
| Units: mg/dL | | | |
| arithmetic mean | 98.67 | 99.54 | |
| standard deviation | ± 35.28 | ± 33.57 | - |
| Fasting Lipids - Non-HDL Cholesterol | | | |
| Mean concentrations of non high-density lipoprotein (HDL) cholesterol. All randomized participants who received at least one dose of study treatment were analyzed | | | |
| Units: mg/dL | | | |
| arithmetic mean | 118.73 | 117.76 | |
| standard deviation | ± 36.93 | ± 37.83 | - |
| Fasting Lipids - Cholesterol | | | |
| Mean concentrations of cholesterol. All randomized participants who received at least one dose of study treatment were analyzed. | | | |
| Units: mg/dL | | | |
| arithmetic mean | 178.11 | 173.02 | |
| standard deviation | ± 36.39 | ± 36.62 | - |
| Fasting Lipids - HDL Cholesterol | | | |
| Mean concentrations of HDL cholesterol. All randomized participants who received at least one dose of study treatment. | | | |
| Units: mg/dL | | | |
| arithmetic mean | 59.38 | 55.27 | |
| standard deviation | ± 14.58 | ± 14.00 | - |
| Fasting Lipids - Triglyceride | | | |
| Mean concentrations of triglyceride. All randomized participants who received at least one dose of study treatment. | | | |
| Units: mg/dL | | | |
| arithmetic mean | 107.49 | 91.39 | |
| standard deviation | ± 65.64 | ± 39.43 | - |

End points

End points reporting groups

| | |
|--|------------------------------|
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |
| Reporting group title | Immediate Switch to MK-1439A |
| Reporting group description: | |
| Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks. Eligible participants from Base Study (Day 1 to Week 24) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 24 to 120), Extension 2 (Weeks 120 to 216), and Extension 3 (Weeks 216 to 312). | |
| Reporting group title | Deferred Switch to MK-1439A |
| Reporting group description: | |
| Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks (Day 1 to Week 12), followed by open-label MK-1439A orally, once daily for 24 weeks (Weeks 12 to 36). Eligible participants from Base Study (Day 1 to Week 36) may have entered open-label optional study extensions to receive MK-1439A once daily during Study Extension 1 (Weeks 36 to 132), Extension 2 (Weeks 132 to 228), and Extension 3 (Weeks 228 to 324). | |

| | |
|----------------------------|---|
| Subject analysis set title | Combined Treatment Groups: Time of Switch |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.

Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

| | |
|----------------------------|--|
| Subject analysis set title | Combined Treatment Groups: Week 24 Post-Switch |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.

Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Combined Treatment Groups |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.

Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Combined Treatment Groups |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Immediate Switch to MK-1439A: Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening will be switched to blinded MK-1439A orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for an additional 12 weeks.

Deferred Switch to MK-1439A: Participants will continue on their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks, followed by open-label MK-1439A orally, once daily for 24 weeks.

Primary: Percentage of participants with at least one central nervous system (CNS) toxicity of at least grade 2 intensity at week 12

| | |
|-----------------|---|
| End point title | Percentage of participants with at least one central nervous system (CNS) toxicity of at least grade 2 intensity at week 12 |
|-----------------|---|

End point description:

A questionnaire was used to solicit for CNS toxicity based on the following 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; and abnormal dreams. Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. Percentage of participants with at least one CNS toxicity of Grade 2 or higher were recorded, based on the last observation carried forward (LOCF) approach. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed.

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

End point timeframe:

Week 12

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 41.9 | 37.2 | | |

Statistical analyses

| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
|--|--|
| Statistical analysis description: | |
| The Immediate Switch group will be considered statistically significantly smaller than the Delayed Switch group if the upper bound of the 95% confidence interval for the treatment difference is less than 0. | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.331 |
| Method | Miettinen and Nurminen |
| Parameter estimate | Estimated Difference |
| Point estimate | 4.65 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.92 |
| upper limit | 24.85 |

Secondary: Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at week 4

| | |
|--|---|
| End point title | Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at week 4 |
| End point description: | |
| A questionnaire was used to solicit for CNS toxicity based on the following 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; and abnormal dreams. Participants were asked to rate the intensity for each of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. Percentage of participants with at least one CNS toxicity of Grade 2 or higher were recorded, based on the last observation carried forward (LOCF) approach. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Week 4 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 46.5 | 65.1 | | |

Statistical analyses

| | |
|--|--|
| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
| Statistical analysis description: | |
| The Immediate Switch group will be considered statistically significantly smaller than the Delayed Switch group if the upper bound of the 95% confidence interval for the treatment difference is less than 0. | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Estimated Difference |
| Point estimate | -18.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38.14 |
| upper limit | 2.51 |

Secondary: Change from baseline in CNS toxicity score at week 4

| | |
|---|--|
| End point title | Change from baseline in CNS toxicity score at week 4 |
| End point description: | |
| A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing all 10 CNS toxicities & converting to a percentage of the maximum possible sum of intensities. A positive change from baseline score = worsening symptoms. A negative change from baseline score = improvement in symptoms. All randomized participants who received ≥1 dose of study treatment & had baseline data where applicable were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 4 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|---|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Percentage of maximum score | | | | |
| arithmetic mean (confidence interval 95%) | -17.6 (-23.4 to -11.8) | -15.6 (-22.0 to -9.2) | | |

Statistical analyses

| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
|---|--|
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Estimated Difference |
| Point estimate | -2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.5 |
| upper limit | 6.5 |

Secondary: Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at time of switch, and at 24 weeks post-switch for the combined treatment groups

| | |
|-----------------|--|
| End point title | Percentage of participants with at least one CNS toxicity of at least grade 2 intensity at time of switch, and at 24 weeks post-switch for the combined treatment groups |
|-----------------|--|

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity for the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. For the Immediate Switch Group (ISG) time of switch was study Day 1, and week 24 post-switch was week 24. For the Delayed Switch Group (DSG) time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment & had baseline data when applicable. Per protocol, the combined treatment groups were analyzed.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (time of switch) and 24 weeks post-switch | |

| End point values | Combined Treatment Groups: Time of Switch | Combined Treatment Groups: Week 24 Post-Switch | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 86 | 86 | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 68.6 | 30.2 | | |

Statistical analyses

| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
|--|--|
| Statistical analysis description: | |
| Change from time of switch to 24 weeks post-switch: Treatment difference in percent response | |
| Comparison groups | Combined Treatment Groups: Week 24 Post-Switch v Combined Treatment Groups: Time of Switch |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference in Percentage |
| Point estimate | -38.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -51.2 |
| upper limit | -23.8 |

Secondary: Change from baseline in CNS toxicity score at week 12

| End point title | Change from baseline in CNS toxicity score at week 12 |
|---|---|
| End point description: | |
| <p>A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity of the 10 events as none (Grade 0), mild (Grade 1), moderate (Grade 2), or severe (Grade 3). Mild = symptom is noticeable but does not interfere with normal activities; moderate = symptom has some impact on normal activities; severe = symptom prevents conduct of normal activities. The CNS toxicity score was calculated by summing all 10 CNS toxicities & converting to a percentage of the maximum possible sum of intensities. A positive change from baseline score = worsening symptoms. A negative change from baseline score = improvement in symptoms. All randomized participants who received ≥ 1 dose of study treatment & had baseline data where applicable were analyzed.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and Week 12 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|---|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Percentage of maximum score | | | | |
| arithmetic mean (confidence interval 95%) | -18.1 (-22.9 to -13.3) | -21.7 (-27.9 to -15.5) | | |

Statistical analyses

| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
|---|--|
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 86 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Estimated Difference |
| Point estimate | 3.6 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -4.1 |
| upper limit | 11.3 |

Secondary: Change from baseline in fasting lipids at week 12

| | |
|------------------------|---|
| End point title | Change from baseline in fasting lipids at week 12 |
| End point description: | Blood was collected under fasting conditions on Day 1 and on week 12 in order to determine the concentration of the following lipids: low-density lipoprotein (LDL) cholesterol; Non high-density lipoprotein (HDL) cholesterol; cholesterol; HDL cholesterol; and triglyceride. All randomized participants who received at least one dose of study treatment, and have required lipid data were analyzed. |
| End point type | Secondary |
| End point timeframe: | Baseline (study Day 1) and study week 12 |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|--------------------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 37 | 41 | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| LDL Cholesterol | -10.78 (± 15.85) | -1.88 (± 14.88) | | |
| Non-HDL Cholesterol | -14.08 (± 17.17) | -0.37 (± 16.51) | | |

| | | | | |
|-----------------|-----------------------|---------------------|--|--|
| Cholesterol | -22.14 (\pm 19.49) | 0.00 (\pm 18.04) | | |
| HDL Cholesterol | -8.05 (\pm 7.74) | 0.37 (\pm 7.91) | | |
| Triglyceride | -21.19 (\pm 43.37) | 7.10 (\pm 38.55) | | |

Statistical analyses

| Statistical analysis title | Difference Estimate: LDL Cholesterol |
|--|--|
| Statistical analysis description: The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference Estimate |
| Point estimate | -9.02 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -15.69 |
| upper limit | -2.35 |

| Statistical analysis title | Difference Estimate: Non-HDL Cholesterol |
|--|--|
| Statistical analysis description: The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference Estimate |
| Point estimate | -13.57 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -20.79 |
| upper limit | -6.35 |

| Statistical analysis title | Difference Estimate: Triglyceride |
|--|-----------------------------------|
| Statistical analysis description: The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment | |

| | |
|---|--|
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference Estimate |
| Point estimate | -22.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -38.52 |
| upper limit | -5.84 |

| | |
|--|--|
| Statistical analysis title | Difference Estimate: HDL Cholesterol |
| Statistical analysis description: The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference Estimate |
| Point estimate | -8.18 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.76 |
| upper limit | -4.6 |

| | |
|--|--|
| Statistical analysis title | Difference Estimate: Cholesterol |
| Statistical analysis description: The 95% CI for treatment difference was calculated from an ANCOVA model with terms for baseline lipid level, use of lipid lowering therapy at study Day 1 and treatment | |
| Comparison groups | Immediate Switch to MK-1439A v Deferred Switch to MK-1439A |
| Number of subjects included in analysis | 78 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Difference Estimate |
| Point estimate | -21.42 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -29.63 |
| upper limit | -13.21 |

Secondary: CNS toxicity scores at time of switch, and at 24 weeks post-switch for the combined treatment groups

| | |
|-----------------|--|
| End point title | CNS toxicity scores at time of switch, and at 24 weeks post-switch for the combined treatment groups |
|-----------------|--|

End point description:

A questionnaire was used to solicit for CNS toxicity based on 10 events: dizziness; depression/low mood; insomnia/sleeplessness; anxiety/nervousness; confusion; impaired concentration/attention; headache; somnolence/daytime sleepiness; aggressive mood/behavior; & abnormal dreams. Participants were asked to rate the intensity for the 10 events as none (Grade 0) through severe (Grade 3). The CNS toxicity score was calculated by summing across all 10 CNS toxicities and converted to a percentage of the maximum possible sum of intensities. A higher CNS score = worse symptoms. A positive change in CNS score = worsening symptoms. A negative change = improvement in symptoms. For the ISG time of switch was Day 1, and week 24 post-switch was week 24. For the DSG time of switch was week 12, and week 24 post-switch was week 36. All randomized participants who received ≥ 1 dose of study treatment & had baseline data where applicable. Per protocol, the combined treatment groups were analyzed.

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

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

| End point values | Combined Treatment Groups: Time of Switch | Combined Treatment Groups: Week 24 Post-Switch | | |
|---|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 86 | 86 | | |
| Units: Percentage of maximum score | | | | |
| arithmetic mean (confidence interval 95%) | 24.2 (20.5 to 27.9) | 10.7 (8.7 to 12.8) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Treatment Difference: Immediate - Delayed Switch |
|----------------------------|--|

Statistical analysis description:

Change from time of switch to 24 weeks post-switch: Treatment difference in score

| | |
|---|--|
| Comparison groups | Combined Treatment Groups: Time of Switch v Combined Treatment Groups: Week 24 Post-Switch |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Parameter estimate | Mean difference (final values) |
| Point estimate | -13.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -16.8 |
| upper limit | -10.1 |

Secondary: Change in fasting lipids between time of switch and week 24 post-switch for the combined treatment groups

| | |
|-----------------|---|
| End point title | Change in fasting lipids between time of switch and week 24 post-switch for the combined treatment groups |
|-----------------|---|

End point description:

Blood was collected under fasting conditions at time of switch and 24 weeks post-switch in order to determine the change from baseline of the following lipids: low-density lipoprotein (LDL) cholesterol; Non high-density lipoprotein (HDL) cholesterol; cholesterol; HDL cholesterol; and triglyceride. For the ISG time of switch was study Day 1, and week 24 post-switch was week 24. For the DSG time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required lipid data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

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

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

| End point values | Combined Treatment Groups | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 76 | | | |
| Units: mg/dL | | | | |
| arithmetic mean (standard deviation) | | | | |
| LDL Cholesterol | -10.97 (± 17.15) | | | |
| Non-HDL Cholesterol | -13.18 (± 19.82) | | | |
| Cholesterol | -20.91 (± 20.19) | | | |
| HDL Cholesterol | -7.72 (± 9.53) | | | |
| Triglyceride | -12.99 (± 46.61) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA <50 and <40 copies/ml at week 24 post-switch for the combined treatment groups

| | |
|-----------------|--|
| End point title | Percentage of participants with HIV-1 RNA <50 and <40 copies/ml at week 24 post-switch for the combined treatment groups |
|-----------------|--|

End point description:

Blood was collected under fasting conditions at 24 weeks post-switch in order to determine the HIV-1 RNA. For the ISG week 24 post-switch was week 24. For the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required HIV-1 RNA data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

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

End point timeframe:
24 weeks post-switch

| End point values | Combined Treatment Groups | | | |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| < 50 copies/mL | 95.3 (88.4 to 98.7) | | | |
| < 40 copies/mL | 95.3 (88.4 to 98.7) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from time of switch to week 24 post switch in CD4 T-cell count for the combined treatment groups

| | |
|-----------------|---|
| End point title | Change from time of switch to week 24 post switch in CD4 T-cell count for the combined treatment groups |
|-----------------|---|

End point description:

Blood was collected at time of switch and at 24 weeks post-switch in order to determine the CD4 T-cell count. For the ISG time of switch was study Day 1, and week 24 post-switch was week 24. For the DSG time of switch was study week 12, and week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have required CD4 T-cell data. Based on the protocol-specified plan, the combined treatment groups was analyzed.

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

End point timeframe:

Baseline (time of switch) and 24 weeks post-switch

| End point values | Combined Treatment Groups | | | |
|---|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: cells/mm ³ | | | | |
| arithmetic mean (confidence interval 95%) | 70.4 (35.9 to 104.8) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related AEs through study week 12

| | |
|-----------------|--|
| End point title | Number of participants with one or more drug-related AEs through study week 12 |
|-----------------|--|

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. A drug-related AE was determined by the investigator to be related to the drug. All randomized participants who received at least one dose of study treatment were analyzed.

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

End point timeframe:

Up to Week 12

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Participants | 14 | 9 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more Serious Adverse Events (SAEs) through study week 12

| | |
|-----------------|---|
| End point title | Number of participants with one or more Serious Adverse Events (SAEs) through study week 12 |
|-----------------|---|

End point description:

A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. All randomized participants who received at least one dose of study treatment were analyzed.

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

End point timeframe:

Up to Week 12

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more Adverse Events (AEs) through study week 12

| | |
|---|--|
| End point title | Number of participants with one or more Adverse Events (AEs) through study week 12 |
| End point description: An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. All randomized participants who received at least one dose of study treatment were analyzed. | |
| End point type | Secondary |
| End point timeframe: Up to Week 12 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Participants | 34 | 34 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related SAEs through study week 12

| | |
|--|---|
| End point title | Number of participants with one or more drug-related SAEs through study week 12 |
| End point description: A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. A drug-related | |

SAE was determined by the investigator to be related to the drug. All randomized participants who received at least one dose of study treatment were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 12 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued treatment due to an AE through study week 12

| | |
|-----------------|--|
| End point title | Number of participants who discontinued treatment due to an AE through study week 12 |
|-----------------|--|

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. All randomized participants who received at least one dose of study treatment were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 12 | |

| End point values | Immediate Switch to MK-1439A | Deferred Switch to MK-1439A | | |
|-----------------------------|------------------------------|-----------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 43 | 43 | | |
| Units: Participants | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related AEs for the combined treatment groups 24 weeks after the switch

| | |
|-----------------|--|
| End point title | Number of participants with one or more drug-related AEs for the combined treatment groups 24 weeks after the switch |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product & which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable & unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. A drug-related AE was determined by the investigator to be related to the drug. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥ 1 dose of study treatment, & have baseline data for analyses requiring baseline data. Per protocol, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

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

End point timeframe:

24 weeks post-switch

| | | | | |
|-----------------------------|---------------------------|--|--|--|
| End point values | Combined Treatment Groups | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Participants | 18 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more AEs for the combined treatment groups 24 weeks after the switch

| | |
|-----------------|---|
| End point title | Number of participants with one or more AEs for the combined treatment groups 24 weeks after the switch |
|-----------------|---|

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product or protocol - specified procedure, whether or not considered related to the medicinal product or protocol - specified procedure. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥ 1 dose of study treatment, and have baseline data for analyses requiring baseline data were analyzed. Per protocol, the combined treatment group was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

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

End point timeframe:

24 weeks post-switch

| End point values | Combined Treatment Groups | | | |
|-----------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Participants | 71 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more drug-related SAEs for the combined treatment groups 24 weeks after the switch

| | |
|--|---|
| End point title | Number of participants with one or more drug-related SAEs for the combined treatment groups 24 weeks after the switch |
| End point description: | |
| A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. A drug-related SAE was determined by the investigator to be related to the drug. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis. | |
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks post-switch | |

| End point values | Combined Treatment Groups | | | |
|-----------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with one or more SAEs for the combined treatment groups 24 weeks after the switch

| | |
|--|--|
| End point title | Number of participants with one or more SAEs for the combined treatment groups 24 weeks after the switch |
| End point description: | |
| A serious adverse event (SAE) is any AE occurring at any dose or during any use of Sponsor's product that results in any of the following: death; is life threatening; results in persistent or significant disability/incapacity; results in or prolongs an existing hospitalization; is a congenital anomaly/birth defect; is another important medical event; is a cancer; is associated with an overdose. For the ISG 24 | |

week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received at least one dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks post-switch | |

| End point values | Combined Treatment Groups | | | |
|-----------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Participants | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who discontinued treatment due to an AE for the combined treatment groups 24 weeks after the switch

| | |
|-----------------|--|
| End point title | Number of participants who discontinued treatment due to an AE for the combined treatment groups 24 weeks after the switch |
|-----------------|--|

End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any worsening of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. For the ISG 24 week post-switch was week 24; for the DSG week 24 post-switch was week 36. All randomized participants who received ≥ 1 dose of study treatment, and have baseline data for analyses requiring baseline data. Based on the protocol-specified plan, the combined treatment groups was analyzed. One participant in the DSG who discontinued from the study, before switching to MK-1439A, was not included in the analysis.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 24 weeks post-switch | |

| End point values | Combined Treatment Groups | | | |
|-----------------------------|---------------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 85 | | | |
| Units: Participants | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 326 weeks

Adverse event reporting additional description:

All cause-mortality was reported on all allocated participants. AEs were reported for all allocated participants who received ≥ 1 dose of study treatment. Per protocol, serious adverse events and all-cause mortality were collected up to 326 weeks, and non-serious adverse event data were collected up to 134 weeks.

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---|
| Reporting group title | Immediate Switch Group Day 1 to Week 24 |
|-----------------------|---|

Reporting group description:

Participants on a baseline regimen of ATRIPLA™ for at least 12 weeks prior to screening switched to blinded doravirine, tenofovir, lamivudine orally, once daily for 12 weeks, followed by open-label doravirine, tenofovir, lamivudine orally, once daily for an additional 12 weeks

| | |
|-----------------------|---|
| Reporting group title | Deferred Switch Group Double-blind Day 1 to Week 12 |
|-----------------------|---|

Reporting group description:

Participants continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks.

| | |
|-----------------------|---|
| Reporting group title | Deferred Switch Group Open-label Week 12-36 |
|-----------------------|---|

Reporting group description:

Participants who continued their ongoing ATRIPLA™ regimen orally, once daily for 12 weeks switched to open-label doravirine, tenofovir, lamivudine orally, once daily for a total of 24 weeks (Week 12 - Week 36).

| | |
|-----------------------|---|
| Reporting group title | Immediate Switch Group only (Week 24-120) EXT 1 |
|-----------------------|---|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 24 - Week 120)

| | |
|-----------------------|---|
| Reporting group title | Deferred Switch Group (Week 36-132) EXT 1 |
|-----------------------|---|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 36 - Week 132)

| | |
|-----------------------|--|
| Reporting group title | Deferred Switch Group (Week 132-228) EXT 2 |
|-----------------------|--|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 132 - Week 228)

| | |
|-----------------------|---|
| Reporting group title | Immediate Switch Group (Week 120-216) EXT 2 |
|-----------------------|---|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 120 - Week 216)

| | |
|-----------------------|---|
| Reporting group title | Immediate Switch Group (Week 216-312) EXT 3 |
|-----------------------|---|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 216 - Week 312)

| | |
|-----------------------|--|
| Reporting group title | Deferred Switch Group (Week 228-324) EXT 3 |
|-----------------------|--|

Reporting group description:

One doravirine, tenofovir, lamivudine taken q.d. by mouth for an additional 96 weeks (Week 228 - Week 324)

| Serious adverse events | Immediate Switch Group Day 1 to Week 24 | Deferred Switch Group Double-blind Day 1 to Week 12 | Deferred Switch Group Open-label Week 12-36 |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 42 (2.38%) |
| 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) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 | | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 1 / 42 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 | | | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 hernia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 | | | |
| Conversion disorder | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 haemophilus | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 |
| Wound sepsis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 43 (0.00%) | 0 / 42 (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 | Immediate Switch Group only (Week 24-120) EXT 1 | Deferred Switch Group (Week 36-132) EXT 1 | Deferred Switch Group (Week 132-228) EXT 2 |
|--|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 2 / 41 (4.88%) | 1 / 33 (3.03%) |
| 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) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 33 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (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 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Spinal compression fracture | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 33 (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 |
| Head injury | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 33 (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 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 33 (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 | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (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 | | | |
| Ectopic pregnancy | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal hernia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (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 |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 0 / 33 (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 | | | |
| Conversion disorder | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (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 | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 1 / 33 (3.03%) |
| 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 haemophilus | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 41 (2.44%) | 0 / 33 (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 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 0 / 41 (0.00%) | 0 / 33 (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 |
| Wound sepsis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 0 / 41 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Immediate Switch Group (Week 120-216) EXT 2 | Immediate Switch Group (Week 216-312) EXT 3 | Deferred Switch Group (Week 228-324) EXT 3 |
|---|---|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 39 (7.69%) | 2 / 17 (11.76%) | 0 / 19 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (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 |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 17 (0.00%) | 0 / 19 (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 |
| Uterine leiomyoma | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 | | | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 |
| Head injury | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 1 / 17 (5.88%) | 0 / 19 (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 |
| Stab wound | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 | | | |
| Ectopic pregnancy | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 hernia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 |
| Reproductive system and breast disorders | | | |
| Cystocele | | | |
| subjects affected / exposed | 1 / 39 (2.56%) | 1 / 17 (5.88%) | 0 / 19 (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 |
| Psychiatric disorders | | | |
| Conversion disorder | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 haemophilus | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 |
| Viral infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 |
| Wound sepsis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (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 |

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

| Non-serious adverse events | Immediate Switch Group Day 1 to Week 24 | Deferred Switch Group Double-blind Day 1 to Week 12 | Deferred Switch Group Open-label Week 12-36 |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 43 (67.44%) | 25 / 43 (58.14%) | 26 / 42 (61.90%) |
| Nervous system disorders | | | |
| Disturbance in attention | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 4 / 43 (9.30%) | 4 / 42 (9.52%) |
| occurrences (all) | 4 | 4 | 4 |
| Somnolence | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 3 / 43 (6.98%) | 5 / 42 (11.90%) |
| occurrences (all) | 8 | 3 | 5 |
| Headache | | | |
| subjects affected / exposed | 11 / 43 (25.58%) | 7 / 43 (16.28%) | 3 / 42 (7.14%) |
| occurrences (all) | 13 | 9 | 3 |
| Dizziness | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | 5 / 43 (11.63%) | 5 / 42 (11.90%) |
| occurrences (all) | 7 | 5 | 5 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 1 / 43 (2.33%) | 0 / 42 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 3 / 43 (6.98%) | 4 / 42 (9.52%) |
| occurrences (all) | 6 | 3 | 4 |
| Nausea | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 5 | 1 / 43 (2.33%) 1 | 1 / 42 (2.38%) 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 2 / 43 (4.65%) | 0 / 42 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Cough | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 0 / 43 (0.00%) | 2 / 42 (4.76%) |
| occurrences (all) | 2 | 0 | 2 |
| Skin and subcutaneous tissue disorders | | | |
| Pruritus | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 1 / 43 (2.33%) | 1 / 42 (2.38%) |
| occurrences (all) | 4 | 1 | 1 |
| Psychiatric disorders | | | |
| Abnormal dreams | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 3 / 43 (6.98%) | 3 / 42 (7.14%) |
| occurrences (all) | 5 | 3 | 3 |
| Aggression | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 2 / 43 (4.65%) | 2 / 42 (4.76%) |
| occurrences (all) | 4 | 2 | 2 |
| Anxiety | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 2 / 43 (4.65%) | 7 / 42 (16.67%) |
| occurrences (all) | 3 | 2 | 7 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 1 / 43 (2.33%) | 3 / 42 (7.14%) |
| occurrences (all) | 1 | 1 | 3 |
| Depressed mood | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 2 / 43 (4.65%) | 0 / 42 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | 7 / 43 (16.28%) | 6 / 42 (14.29%) |
| occurrences (all) | 9 | 10 | 6 |
| Depression | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | 1 / 43 (2.33%) | 4 / 42 (9.52%) |
| occurrences (all) | 3 | 1 | 4 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|----------------------|----------------------|---------------------|
| Back pain subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 4 | 1 / 43 (2.33%) 1 | 1 / 42 (2.38%) 1 |
| Arthralgia subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 8 | 1 / 43 (2.33%) 1 | 2 / 42 (4.76%) 2 |
| Infections and infestations | | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 2 / 43 (4.65%) 2 | 2 / 42 (4.76%) 2 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 6 | 6 / 43 (13.95%) 6 | 2 / 42 (4.76%) 2 |
| Viral infection subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | 0 / 43 (0.00%) 0 | 0 / 42 (0.00%) 0 |
| Lower respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 43 (2.33%) 1 | 0 / 42 (0.00%) 0 |
| Viral upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 0 / 43 (0.00%) 0 | 1 / 42 (2.38%) 1 |
| Gastroenteritis subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 | 0 / 43 (0.00%) 0 | 0 / 42 (0.00%) 0 |
| Influenza subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 0 / 43 (0.00%) 0 | 2 / 42 (4.76%) 2 |

| Non-serious adverse events | Immediate Switch Group only (Week 24-120) EXT 1 | Deferred Switch Group (Week 36- 132) EXT 1 | Deferred Switch Group (Week 132- 228) EXT 2 |
|--|---|--|---|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 31 / 43 (72.09%) | 33 / 41 (80.49%) | 0 / 33 (0.00%) |
| Nervous system disorders Disturbance in attention subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 5 | 5 / 41 (12.20%) 5 | 0 / 33 (0.00%) 0 |

| | | | |
|---|--|--|--|
| Somnolence subjects affected / exposed occurrences (all) | 9 / 43 (20.93%) 9 | 7 / 41 (17.07%) 9 | 0 / 33 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 8 / 43 (18.60%) 8 | 14 / 41 (34.15%) 15 | 0 / 33 (0.00%) 0 |
| Dizziness subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 5 | 5 / 41 (12.20%) 5 | 0 / 33 (0.00%) 0 |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | 4 / 41 (9.76%) 4 | 0 / 33 (0.00%) 0 |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 | 4 / 41 (9.76%) 4 2 / 41 (4.88%) 2 | 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 3 / 43 (6.98%) 3 | 1 / 41 (2.44%) 1 2 / 41 (4.88%) 2 | 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | 1 / 41 (2.44%) 1 | 0 / 33 (0.00%) 0 |
| Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all) Aggression | 5 / 43 (11.63%) 6 | 5 / 41 (12.20%) 5 | 0 / 33 (0.00%) 0 |

| | | | |
|---|-----------------|------------------|----------------|
| subjects affected / exposed | 4 / 43 (9.30%) | 7 / 41 (17.07%) | 0 / 33 (0.00%) |
| occurrences (all) | 4 | 7 | 0 |
| Anxiety | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | 11 / 41 (26.83%) | 0 / 33 (0.00%) |
| occurrences (all) | 7 | 11 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | 6 / 41 (14.63%) | 0 / 33 (0.00%) |
| occurrences (all) | 6 | 7 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 2 / 41 (4.88%) | 0 / 33 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 10 / 41 (24.39%) | 0 / 33 (0.00%) |
| occurrences (all) | 5 | 13 | 0 |
| Depression | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 8 / 41 (19.51%) | 0 / 33 (0.00%) |
| occurrences (all) | 7 | 8 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | 2 / 41 (4.88%) | 0 / 33 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | 3 / 41 (7.32%) | 0 / 33 (0.00%) |
| occurrences (all) | 4 | 3 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | 2 / 41 (4.88%) | 0 / 33 (0.00%) |
| occurrences (all) | 5 | 5 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | 7 / 41 (17.07%) | 0 / 33 (0.00%) |
| occurrences (all) | 5 | 8 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | 3 / 41 (7.32%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Lower respiratory tract infection | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 4 / 43 (9.30%) | 4 / 41 (9.76%) | 0 / 33 (0.00%) |
| occurrences (all) | 4 | 4 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | 3 / 41 (7.32%) | 0 / 33 (0.00%) |
| occurrences (all) | 3 | 5 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | 2 / 41 (4.88%) | 0 / 33 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Influenza | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | 0 / 41 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |

| Non-serious adverse events | Immediate Switch Group (Week 120-216) EXT 2 | Immediate Switch Group (Week 216-312) EXT 3 | Deferred Switch Group (Week 228-324) EXT 3 |
|---|---|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| Nervous system disorders | | | |
| Disturbance in attention | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|---|---|---|
| Nausea subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 | 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 | 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 | 0 / 17 (0.00%) 0 | 0 / 19 (0.00%) 0 |
| Psychiatric disorders Abnormal dreams subjects affected / exposed occurrences (all) Aggression subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all) Depressed mood subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all) | 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 0 / 39 (0.00%) 0 | 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 0 / 17 (0.00%) 0 | 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 |

| | | | |
|---|----------------|----------------|----------------|
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 39 (0.00%) | 0 / 17 (0.00%) | 0 / 19 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 13 October 2016 | The primary purpose of Amendment 1 was to add study extension 1 to collect long-term efficacy and safety data and to incorporate changes to facilitate enrollment and ensure trial completion. |
| 13 July 2018 | The primary purpose of Amendment 2 was to add study extension 2 to provide continued access to MK-1439A for participants who are deriving benefit from MK-1439A until the drug is available locally in the country participating in the trial or for an additional 2 years. |
| 18 March 2021 | The primary purpose of Amendment 3 was to provide continued access to MK-1439A until the drug is available locally in countries participating in the trial or for an additional 2 years (whichever comes first). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported