



Clinical trial results:

A Phase 3b, Randomized, Open-Label Study to Evaluate the Safety and Efficacy of Switching From Regimens Consisting of Abacavir/Lamivudine (ABC/3TC) Plus a Third Antiretroviral Agent to the Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (E/C/F/TAF) Fixed-Dose Combination (FDC) in Virologically-Suppressed HIV 1 Infected Adult Subjects

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2015-002711-15 |
| Trial protocol | GB DE ES IT |
| Global end of trial date | 24 January 2018 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 29 June 2018 |
| First version publication date | 29 June 2018 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | GS-US-292-1823 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02605954 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Gilead Sciences |
| Sponsor organisation address | 333 Lakeside Drive, Foster City, CA, United States, 94404 |
| Public contact | Gilead Clinical Study Information Center , Gilead Sciences, GileadClinicalTrials@gilead.com |
| Scientific contact | Gilead Clinical Study Information Center , Gilead Sciences, GileadClinicalTrials@gilead.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 | 24 January 2018 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 June 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 January 2018 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the efficacy of switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) fixed-dose combination (FDC) relative to continuing on a baseline regimen consisting of abacavir/lamivudine (ABC/3TC) plus a 3rd antiretroviral agent in HIV-1 infected participants.

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 18 November 2015 |
| 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 | United States: 56 |
| Country: Number of subjects enrolled | Italy: 59 |
| Country: Number of subjects enrolled | Spain: 86 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | France: 63 |
| Country: Number of subjects enrolled | Germany: 8 |
| Worldwide total number of subjects | 275 |
| EEA total number of subjects | 219 |

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) | 247 |
| From 65 to 84 years | 28 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in Europe and North America. The first participant was screened on 18 November 2015. The last study visit occurred on 24 Jan 2018.

Pre-assignment

Screening details:

346 participants were screened.

Period 1

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

Arms

| | |
|------------------------------|-----------|
| Are arms mutually exclusive? | Yes |
| Arm title | E/C/F/TAF |

Arm description:

Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide |
| Investigational medicinal product code | |
| Other name | E/C/F/TAF |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

150/150/200/10 mg administered once daily with food for 48 weeks

| | |
|------------------|-------------------|
| Arm title | ABC/3TC+3rd Agent |
|------------------|-------------------|

Arm description:

Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC

| | |
|--|--------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Abacavir/lamivudine |
| Investigational medicinal product code | |
| Other name | ABC/3TC, Epzicom, Kivexa |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

600/300 mg plus a third antiretroviral agent administered orally once daily for 24 weeks

| Number of subjects in period 1^[1] | E/C/F/TAF | ABC/3TC+3rd Agent |
|---|------------------|--------------------------|
| Started | 183 | 91 |
| Completed | 171 | 88 |
| Not completed | 12 | 3 |
| Withdrew Consent | 2 | 2 |
| Non-Compliance with Study Drug | 1 | - |
| Adverse event, non-fatal | 5 | 1 |
| Lost to Follow-up | 3 | - |
| Investigator's Discretion | 1 | - |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 1 participant who was randomized/enrolled but not treated is not included in the subject disposition table.

Baseline characteristics

Reporting groups

| | |
|--|-------------------|
| Reporting group title | E/C/F/TAF |
| Reporting group description: Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks | |
| Reporting group title | ABC/3TC+3rd Agent |
| Reporting group description: Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC | |

| Reporting group values | E/C/F/TAF | ABC/3TC+3rd Agent | Total |
|---|-----------|-------------------|-------|
| Number of subjects | 183 | 91 | 274 |
| Age categorical Units: Subjects | | | |
| Age continuous | | | |
| Safety Analysis Set: participants who took at least 1 dose of E/C/F/TAF or ABC/3TC+3rd Agent (on or after Day 1). | | | |
| Units: years | | | |
| arithmetic mean | 50 | 49 | |
| standard deviation | ± 11.6 | ± 10.7 | - |
| Gender categorical Units: Subjects | | | |
| Female | 27 | 17 | 44 |
| Male | 156 | 74 | 230 |
| Race Units: Subjects | | | |
| Asian | 5 | 1 | 6 |
| Black | 27 | 15 | 42 |
| White | 150 | 75 | 225 |
| Other | 1 | 0 | 1 |
| Ethnicity Units: Subjects | | | |
| Hispanic or Latino | 27 | 16 | 43 |
| Not Hispanic or Latino | 155 | 73 | 228 |
| Not Permitted | 1 | 2 | 3 |
| HIV-1 RNA Categories Units: Subjects | | | |
| < 50 copies/mL | 177 | 91 | 268 |
| 50 ≥ copies/mL | 6 | 0 | 6 |
| CD4 Cell Count Category Units: Subjects | | | |
| ≥ 50 to < 200 cells/μL | 2 | 0 | 2 |
| ≥ 200 to < 350 cells/μL | 11 | 7 | 18 |
| ≥ 350 to < 500 cells/μL | 30 | 13 | 43 |
| ≥ 500 cells/μL | 140 | 71 | 211 |

| | | | |
|-----------------------|-------------|-------------|---|
| CD4 Cell Count | | | |
| Units: cells/ μ L | | | |
| arithmetic mean | 701 | 753 | |
| standard deviation | ± 280.1 | ± 312.8 | - |

End points

End points reporting groups

| | |
|--|-------------------|
| Reporting group title | E/C/F/TAF |
| Reporting group description: Elvitegravir/ cobicistat/ emtricitabine/tenofovir alafenamide (E/C/F/TAF) 150/150/200/10 mg fixed dose combination (FDC) tablets administered orally once daily with food for 48 weeks | |
| Reporting group title | ABC/3TC+3rd Agent |
| Reporting group description: Abacavir/lamivudine (ABC/3TC) 600/300 mg tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC | |
| Subject analysis set title | Delayed E/C/F/TAF |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants in 'ABC/3TC+3rd agent' group who switched to E/C/F/TAF group at Week 24 received E/C/F/TAF (150/150/200/10 mg) FDC tablets orally once daily with food | |

Primary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 24

| | |
|--|--|
| End point title | Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 24 |
| End point description: <ul style="list-style-type: none">The percentage of participants achieving HIV-1 RNA < 50 copies/mL at Week 24 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.Full Analysis Set: participants who were randomized and received at least one dose of study drug (either E/C/F/TAF or ABC/3TC+3rd agent on or after Day 1). | |
| End point type | Primary |
| End point timeframe: Week 24 | |

| End point values | E/C/F/TAF | ABC/3TC+3rd Agent | Delayed E/C/F/TAF | |
|-----------------------------------|-----------------|-------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 183 | 91 | 89 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 93.4 | 97.8 | 96.6 | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent |
| Comparison groups | E/C/F/TAF v ABC/3TC+3rd Agent |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 274 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[1] |
| P-value | = 0.15 |
| Method | Fisher exact |
| Parameter estimate | Difference in Percentages |
| Point estimate | -4.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.4 |
| upper limit | 1.9 |

Notes:

[1] - With 200 participants randomized to switch to the E/C/F/TAF FDC group at Day 1 and 100 participants randomized to the ABC/3TC+3rd Agent group at Week 24, the lower limit of the observed one sided 97.5% confidence interval was expected to be greater than -0.120 (ie, non-inferiority margin of 12%) with > 90% power when the percentage of responders in both treatment groups for the primary endpoint is at least 90% at Week 24.

Secondary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 12

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 12 |
|-----------------|--|

End point description:

- The percentage of participants achieving HIV-1 RNA < 50 copies/mL at week 12 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.

- Full Analysis Set

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

| End point values | E/C/F/TAF | ABC/3TC+3rd Agent | Delayed E/C/F/TAF | |
|-----------------------------------|-----------------|-------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 183 | 91 | 89 | |
| Units: percentage of participants | | | | |
| number (not applicable) | 95.1 | 98.9 | 96.6 | |

Statistical analyses

| | |
|-----------------------------------|---|
| Statistical analysis title | Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent |
| Comparison groups | E/C/F/TAF v ABC/3TC+3rd Agent |

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 274 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| P-value | = 0.17 |
| Method | Fisher exact |
| Parameter estimate | Difference in Percentages |
| Point estimate | -3.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.3 |
| upper limit | 1.6 |

Notes:

[2] - With 200 participants randomized to switch to the E/C/F/TAF FDC group at Day 1 and 100 participants randomized to the delayed switch group at Week 12, the lower limit of the observed one sided 97.5% confidence interval will be expected to be greater than -0.120 (ie, non-inferiority margin of 12%) with > 90% power when the percentage of responders in both treatment groups for the primary endpoint is at least 90% at Week 12.

Secondary: Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 48

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Have HIV-1 RNA < 50 Copies/mL as Defined by the FDA Snapshot Algorithm at Week 48 ^[3] |
|-----------------|---|

End point description:

- The percentage of participants achieving HIV-1 RNA < 50 copies/mL at week 48 was analyzed using the snapshot algorithm, which defines a participant's virologic response status using only the viral load at the predefined time point within an allowed window of time, along with study drug discontinuation status.
- Only the participants who were randomized to E/C/F/TAF group were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only participants who were randomized to E/C/F/TAF group were analyzed.

| End point values | E/C/F/TAF | | | |
|-----------------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 183 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 86.9 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count at Week 24

| | |
|-----------------|--|
| End point title | Change From Baseline in CD4+ Cell Count at Week 24 |
|-----------------|--|

End point description:

Participants in the Full Analysis Set with available data were analyzed.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline; Week 24 | |

| End point values | E/C/F/TAF | ABC/3TC+3rd Agent | Delayed E/C/F/TAF | |
|--------------------------------------|--------------------|-------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 169 | 90 | 86 | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | -28 (\pm 161.4) | 8 (\pm 192.9) | -23 (\pm 201.7) | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Stats Analysis – E/C/F/TAF vs ABC/3TC+3rd agent |
| Comparison groups | E/C/F/TAF v ABC/3TC+3rd Agent |
| Number of subjects included in analysis | 259 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | = 0.11 |
| Method | ANOVA |
| Parameter estimate | Difference in least square mean |
| Point estimate | -36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -80 |
| upper limit | 9 |

Secondary: Change From Baseline in CD4+ Cell Count at Week 48

| | |
|--|---|
| End point title | Change From Baseline in CD4+ Cell Count at Week 48 ^[4] |
| End point description: | |
| Participants in the E/C/F/TAF group with available data were analyzed. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline; Week 48 | |

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only the participants who were randomized to E/C/F/TAF group were analyzed.

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | E/C/F/TAF | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 156 | | | |
| Units: cells/ μ L | | | | |
| arithmetic mean (standard deviation) | -32 (\pm 147.1) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 48 weeks plus 30 days

Adverse event reporting additional description:

The reported percentages in the Adverse Events table were not adjusted for the different durations in adverse events (AE) collection. By study design, the AE collection time frame for the treatment groups was as follows:

- E/C/F/TAF group = 48 weeks plus 30 days
- ABC/3TC+3rd Agent = 24 weeks
- Delayed E/C/F/TAF group = 24 weeks plus 30 days

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------|
| Reporting group title | E/C/F/TAF |
|-----------------------|-----------|

Reporting group description:

E/C/F/TAF (150/150/200/10 mg) FDC tablets administered orally once daily with food for 48 weeks

| | |
|-----------------------|-------------------|
| Reporting group title | ABC/3TC+3rd Agent |
|-----------------------|-------------------|

Reporting group description:

ABC/3TC (600/300 mg) tablets plus a third antiretroviral agent administered orally once daily for 24 weeks followed by a delayed switch to E/C/F/TAF FDC

| | |
|-----------------------|-------------------|
| Reporting group title | Delayed E/C/F/TAF |
|-----------------------|-------------------|

Reporting group description:

Participants in 'ABC/3TC+3rd agent' group who switched to E/C/F/TAF group at Week 24 received E/C/F/TAF (150/150/200/10 mg) FDC tablets orally once daily with food.

| | |
|-----------------------|---------------|
| Reporting group title | All E/C/F/TAF |
|-----------------------|---------------|

Reporting group description:

Adverse events in this reporting group include those that occurred any time during the study by participants while receiving E/C/F/TAF.

Participants received E/C/F/TAF (150/150/200/10 mg) FDC tablets administered orally once daily with food.

| Serious adverse events | E/C/F/TAF | ABC/3TC+3rd Agent | Delayed E/C/F/TAF |
|---|------------------|-------------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 12 / 183 (6.56%) | 1 / 91 (1.10%) | 4 / 89 (4.49%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Deep vein thrombosis | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 183 (0.00%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 183 (1.09%) | 0 / 91 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 183 (0.00%) | 1 / 91 (1.10%) | 0 / 89 (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 |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 183 (0.00%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 183 (0.00%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Ureterolithiasis | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 183 (0.00%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatitis A | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|----------------|
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 183 (0.00%) | 0 / 91 (0.00%) | 1 / 89 (1.12%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 183 (0.55%) | 0 / 91 (0.00%) | 0 / 89 (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 |

| | | | |
|---|------------------|--|--|
| Serious adverse events | All E/C/F/TAF | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 16 / 272 (5.88%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Coronary artery disease | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myocardial infarction | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pericarditis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 272 (0.74%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 0 / 272 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Cervical dysplasia | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ureterolithiasis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 272 (0.74%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Erysipelas | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatitis A | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 1 / 272 (0.37%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | E/C/F/TAF | ABC/3TC+3rd Agent | Delayed E/C/F/TAF |
|---|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 71 / 183 (38.80%) | 21 / 91 (23.08%) | 17 / 89 (19.10%) |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 15 / 183 (8.20%) | 4 / 91 (4.40%) | 4 / 89 (4.49%) |
| occurrences (all) | 21 | 5 | 4 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 10 / 183 (5.46%) | 1 / 91 (1.10%) | 0 / 89 (0.00%) |
| occurrences (all) | 10 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 19 / 183 (10.38%) | 3 / 91 (3.30%) | 4 / 89 (4.49%) |
| occurrences (all) | 22 | 4 | 4 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 11 / 183 (6.01%) | 2 / 91 (2.20%) | 8 / 89 (8.99%) |
| occurrences (all) | 11 | 2 | 8 |
| Back pain | | | |
| subjects affected / exposed | 6 / 183 (3.28%) | 6 / 91 (6.59%) | 2 / 89 (2.25%) |
| occurrences (all) | 6 | 6 | 2 |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 12 / 183 (6.56%) | 5 / 91 (5.49%) | 1 / 89 (1.12%) |
| occurrences (all) | 14 | 5 | 1 |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 13 / 183 (7.10%) | 6 / 91 (6.59%) | 0 / 89 (0.00%) |
| occurrences (all) | 13 | 6 | 0 |

| Non-serious adverse events | All E/C/F/TAF | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 88 / 272 (32.35%) | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 19 / 272 (6.99%) | | |
| occurrences (all) | 25 | | |

| | | | |
|--|--|--|--|
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 10 / 272 (3.68%) 10 | | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 23 / 272 (8.46%) 26 | | |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) | 19 / 272 (6.99%) 19 8 / 272 (2.94%) 8 | | |
| Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) | 13 / 272 (4.78%) 15 | | |
| Metabolism and nutrition disorders Vitamin D deficiency subjects affected / exposed occurrences (all) | 13 / 272 (4.78%) 13 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|---|
| 01 June 2016 | Eligibility criteria updated to allow additional participants to enroll in the study without changing the overall risk/benefit ratio. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported