# Clinical trial results:
# A Phase 4 Trial to Assess the Effectiveness of Apixaban Compared With Usual Care Anticoagulation in Subjects With Nonvalvular Atrial Fibrillation Undergoing Cardioversion

## Summary

| | |
|---|---|
| EudraCT number | 2014-001231-36 |
| Trial protocol | DK ES BE SE DE |
| Global end of trial date | 08 February 2017 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 02 February 2018 |
| First version publication date | 02 February 2018 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | B0661025/CV185-267 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02100228 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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 July 2017 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 February 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the occurrence of clinical endpoints in nonvalvular atrial fibrillation subjects (i.e., without rheumatic mitral valve disease, a prosthetic heart valve, or valve repair) indicated for cardioversion and treated with apixaban or usual care (parenteral heparin and/or oral anticoagulation with vitamin K antagonist, excluding other novel oral anticoagulant).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 14 July 2014 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Belgium: 135 |
| Country: Number of subjects enrolled | Canada: 38 |
| Country: Number of subjects enrolled | Denmark: 70 |
| Country: Number of subjects enrolled | Germany: 320 |
| Country: Number of subjects enrolled | Israel: 295 |
| Country: Number of subjects enrolled | Italy: 55 |
| Country: Number of subjects enrolled | Japan: 49 |
| Country: Number of subjects enrolled | Korea, Republic of: 102 |
| Country: Number of subjects enrolled | Romania: 79 |
| Country: Number of subjects enrolled | Spain: 57 |
| Country: Number of subjects enrolled | Sweden: 84 |
| Country: Number of subjects enrolled | United States: 216 |
| Worldwide total number of subjects | 1500 |
| EEA total number of subjects | 800 |

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) | 679 |
| From 65 to 84 years | 774 |
| 85 years and over | 47 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Fifteen hundred subjects were enrolled at 134 centers. The study was conducted from 14 July 2014 to 08 Feb 2017.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Apixaban |

Arm description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received Apixaban orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of Apixaban was based on investigator's judgement as per local label for the prevention of stroke and systemic embolism in subjects.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Apixaban |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects were administered orally with 2.5 or 5 milligram (mg) of Apixaban twice daily for 30 days following cardioversion or 90 days post randomization if cardioversion was not performed within that timeframe.

| | |
|---|---|
| **Arm title** | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |

Arm description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received parenteral heparin and/or oral Vitamin K antagonist as usual care, orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of the parenteral heparin and Vitamin K antagonist was based on individual subject's sensitivity to the drug according to the investigators usual practice.

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

Dosage and administration details:

Subjects were administered orally with Vitamin K (dosing was based on individual subject's sensitivity to the drug according to the investigators usual practice) for 30 days following cardioversion or 90 days post randomization if cardioversion was not performed within that timeframe.

| | |
|---|---|
| Investigational medicinal product name | Heparin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |

| Routes of administration | Intravenous use |
|---|---|

Dosage and administration details:

Subjects were administered intravenously with Heparin (dosing was based on individual subject's sensitivity to the drug according to the investigators usual practice) for 30 days following cardioversion or 90 days post randomization if cardioversion was not performed within that timeframe.

| **Number of subjects in period 1** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |
|---|---|---|
| Started | 753 | 747 |
| Completed | 678 | 657 |
| Not completed | 75 | 90 |
| Adverse event, serious fatal | 1 | 1 |
| Inclusion/Exclusion criteria not met | 12 | 16 |
| Consent withdrawn by subject | 27 | 37 |
| Adverse event, non-fatal | 16 | 12 |
| Non-compliance | - | 3 |
| Unspecified | 19 | 19 |
| Lost to follow-up | - | 1 |
| Administrative reason | - | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Apixaban |
| Reporting group description: | |
| Subjects with non-valvular atrial fibrillation undergoing cardioversion, received Apixaban orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of Apixaban was based on investigator's judgement as per local label for the prevention of stroke and systemic embolism in subjects. | |
| Reporting group title | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |
| Reporting group description: | |
| Subjects with non-valvular atrial fibrillation undergoing cardioversion, received parenteral heparin and/or oral Vitamin K antagonist as usual care, orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of the parenteral heparin and Vitamin K antagonist was based on individual subject's sensitivity to the drug according to the investigators usual practice. | |

| Reporting group values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | Total |
|---|---|---|---|
| Number of subjects | 753 | 747 | 1500 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 342 | 337 | 679 |
| From 65-84 years | 388 | 386 | 774 |
| 85 years and over | 23 | 24 | 47 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 64.7 | 64.5 | |
| standard deviation | ± 12.19 | ± 12.76 | - |
| Gender, Male/Female<br>Units: Subjects | | | |
| Female | 248 | 250 | 498 |
| Male | 505 | 497 | 1002 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Race: White | 654 | 648 | 1302 |
| Race: Black or African American | 21 | 20 | 41 |
| Race: Asian | 78 | 76 | 154 |
| Race: Other | 0 | 3 | 3 |
| Race/Ethnicity, Customized<br>Units: Subjects | | | |
| Ethnicity: Hispanic or Latino | 8 | 9 | 17 |
| Ethnicity: Not Hispanic or Latino | 100 | 99 | 199 |

| | | | |
|---|---|---|---|
| Ethnicity: Unknown or Not Reported | 645 | 639 | 1284 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Apixaban |

Reporting group description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received Apixaban orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of Apixaban was based on investigator's judgement as per local label for the prevention of stroke and systemic embolism in subjects.

| | |
|---|---|
| Reporting group title | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |

Reporting group description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received parenteral heparin and/or oral Vitamin K antagonist as usual care, orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of the parenteral heparin and Vitamin K antagonist was based on individual subject's sensitivity to the drug according to the investigators usual practice.

### Primary: Number of Subjects With Acute Stroke Event

| | |
|---|---|
| End point title | Number of Subjects With Acute Stroke Event |

End point description:

An acute stroke was defined as a new, important neurological insufficiency of rapid onset that lasted for at least 24 hours and that was not due to a readily identifiable non-vascular cause (like brain tumor or trauma). Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to 30 days post cardio version (or up to 90 days after randomization, if cardio version was not performed within that time frame)

| End point values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 747 | | |
| Units: subjects | 0 | 6 | | |

### Statistical analyses

| Statistical analysis title | Comparison of Apixaban and Usual Care |
|---|---|

Statistical analysis description:

This was a descriptive study, and there was no formal pre-defined hypothesis testing.

| | |
|---|---|
| Comparison groups | Apixaban v Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |

| | |
|---|---|
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 0.0151 |
| Method | Fisher exact |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0 |
| upper limit | 0.6425 |

Notes:

[1] - Display exact confidence limits for relative risk and Fisher's exact test for comparisons of two proportions.

## Primary: Number of Subjects With Systemic Embolism Event

| | |
|---|---|
| End point title | Number of Subjects With Systemic Embolism Event[2] |

End point description:

Systemic embolism occurred in subject when there was a clinical history consistent with an acute loss of blood flow to a peripheral artery (or arteries), which was supported by evidence of embolism from surgical specimens, autopsy, angiography, or other objective testing. Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to 30 days post cardioversion (or up to 90 days after randomization, if cardioversion was not performed within that time frame)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analyses was done for this endpoint since there were no subjects with systemic embolism event.

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 747 | | |
| Units: subjects | | | | |
| number (not applicable) | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Subjects With Major Bleeding Event

| | |
|---|---|
| End point title | Number of Subjects With Major Bleeding Event |

End point description:

Major bleeding was defined as clinically evident bleeding that was accompanied by one or more of the following: a decrease in hemoglobin of 2 gram per deciliter or more, a transfusion of 2 or more units of packed red blood cells, bleeding that was fatal or bleeding that occurred in at least one of the following

critical sites: intracranial, intra-spinal, intraocular (within the corpus of the eye; thus, a conjunctival bleed was not an intraocular bleed), pericardial, intra-articular, intramuscular with compartment syndrome, retroperitoneal. Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to 30 days post cardioversion (or up to 90 days after randomization, if cardioversion was not performed within that time frame)

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 735 | 721 | | |
| Units: subjects | | | | |
| number (not applicable) | 3 | 6 | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of Apixaban and Usual Care |
|---|---|

Statistical analysis description:

This was a descriptive study, and there was no formal pre-defined hypothesis testing.

| Comparison groups | Apixaban v Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |
|---|---|
| Number of subjects included in analysis | 1456 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[3] |
| P-value | = 0.3378 |
| Method | Fisher exact |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.4905 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1046 |
| upper limit | 2.0678 |

Notes:

[3] - Display exact confidence limits for relative risk and Fisher's exact test for comparisons of two proportions.

### Primary: Number of Subjects With Clinically Relevant Non-Major Bleeding Events

| End point title | Number of Subjects With Clinically Relevant Non-Major Bleeding Events |
|---|---|

End point description:

Clinically relevant non-major bleeding was defined as the clinically evident bleeding consisted of any bleeding that compromised hemodynamics, led to hospitalization, subcutaneous hematoma larger than 25/100 centimeter square if there was a traumatic cause, intramuscular hematoma, epistaxis, gingival bleeding, hematuria, macroscopic gastrointestinal hemorrhage with at least one episode of melena or hematemesis, rectal blood loss, hemoptysis or any other bleeding type with clinical consequences for a subject, such as medical intervention, the need for unscheduled contact with a physician, temporary

cessation of a study drug, or associated with pain or impairment of activities of daily life. Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to 30 days post cardioversion (or up to 90 days after randomization, if cardioversion was not performed within that time frame)

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 735 | 721 | | |
| Units: subjects | | | | |
| number (not applicable) | 11 | 13 | | |

### Statistical analyses

| **Statistical analysis title** | Comparison of Apixaban and Usual Care |
|---|---|

Statistical analysis description:

This was a descriptive study, and there was no formal pre-defined hypothesis testing.

| | |
|---|---|
| Comparison groups | Apixaban v Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |
| Number of subjects included in analysis | 1456 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[4] |
| P-value | = 0.6851 |
| Method | Fisher exact |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 0.83 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.3433 |
| upper limit | 1.8916 |

Notes:

[4] - Display exact confidence limits for relative risk and Fisher's exact test for comparisons of two proportions.

### Primary: Number of Subjects With All Cause Death

| End point title | Number of Subjects With All Cause Death |
|---|---|

End point description:

Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to 30 days post cardioversion (or up to 90 days after randomization, if cardioversion was not performed within that time frame)

| End point values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 747 | | |
| Units: subjects | | | | |
| number (not applicable) | 2 | 1 | | |

### Statistical analyses

| Statistical analysis title | Comparison of Apixaban and Usual Care |
|---|---|

Statistical analysis description:

This was a descriptive study, and there was no formal pre-defined hypothesis testing.

| Comparison groups | Apixaban v Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |
|---|---|
| Number of subjects included in analysis | 1500 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[5] |
| P-value | > 0.9999 |
| Method | Fisher exact |
| Parameter estimate | Risk ratio (RR) |
| Point estimate | 1.9841 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.1866 |
| upper limit | 53.9968 |

Notes:

[5] - Display exact confidence limits for relative risk and Fisher's exact test for comparisons of two proportions.

### Secondary: Time to First Attempt of Cardioversion

| End point title | Time to First Attempt of Cardioversion |
|---|---|

End point description:

Cardioversion was an effective method of converting an abnormally fast heart rate (tachycardia) or other cardiac arrhythmia to normal rhythm using electricity or drugs. First attempt of cardioversion was defined as the first time the subject was admitted for the cardioversion procedure. Full analysis set included all randomized subjects. Here "N" signifies number of subjects evaluable for the specified outcome measure.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| End point values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 510 | 511 | | |
| Units: days | | | | |
| median (full range (min-max)) | 2.0 (1 to 93) | 2.0 (1 to 126) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects With Different Type of Cardioversion Events

| End point title | Number of Subjects With Different Type of Cardioversion Events |
|---|---|

End point description:

Cardioversion was an effective method of converting an abnormally fast heart rate (tachycardia) or other cardiac arrhythmia to normal rhythm using different type of cardioversion events i.e. electrical and pharmacologic. Electrical cardioversion was a procedure in which an electric current was used to reset the heart's rhythm back to its regular pattern (normal sinus rhythm). Pharmacologic cardioversion, also called chemical cardioversion, used antiarrhythmia medication instead of an electrical shock. Full analysis set included all randomized subjects. Here "N" signifies number of subjects evaluable for the specified outcome measure.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| End point values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 496 | 494 | | |
| Units: subjects | | | | |
| Electrical | 461 | 464 | | |
| Pharmacologic | 35 | 30 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Cardioversion Attempt of Subjects

| End point title | Number of Cardioversion Attempt of Subjects |
|---|---|

End point description:

Cardioversion attempts were defined as the number of times the subject was admitted to hospital for

the cardioversion procedure and not the number of attempts during a single hospital admission. Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 747 | | |
| Units: subjects | | | | |
| No Cardioversion Attempt | 234 | 224 | | |
| 1 Cardioversion Attempt | 488 | 496 | | |
| More than 2 Cardioversion Attempts | 31 | 27 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Their Rhythm Status

| End point title | Number of Subjects With Their Rhythm Status |
|---|---|

End point description:

Rhythm status was further distinguished into sinus rhythm, atrial fibrillation and atrial flutter. Sinus rhythm was defined as a normal heartbeat. Atrial fibrillation was an irregular heartbeat (arrhythmia) that can lead to blood clots, stroke, heart failure and other heart-related complications and atrial flutter was a common abnormal heart rhythm that was usually associated with a fast heart rate (100 or more heart beats per minute). Safety data set included all treated subjects (randomized subjects who received at least one dose of study drug). Here "N" signifies number of subjects evaluable for the specified outcome measure.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 719 | 712 | | |
| Units: subjects | | | | |
| Normal Sinus | 1 | 2 | | |
| Atrial Fibrillation | 715 | 704 | | |
| Atrial Flutter | 3 | 6 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Duration of Hospital Stay of Subjects

| End point title | Duration of Hospital Stay of Subjects |
|---|---|

End point description:

Duration of hospital stay was defined as the number of hours from hospital admission to hospital discharge followed by early cardioversion. Full analysis set included all randomized subjects. Here "N" signifies number of subjects evaluable for the specified outcome measure.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| **End point values** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 330 | 346 | | |
| Units: hours | | | | |
| median (full range (min-max)) | 45.36 (0.4 to 747.0) | 49.47 (0.6 to 709.6) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects Who Used Image Guidance Approach

| End point title | Number of Subjects Who Used Image Guidance Approach |
|---|---|

End point description:

An image-guided approach helped cardioversion earlier than the conventional minimum of 3 weeks of anticoagulation that would normally be required prior to cardioversion. Transesophageal echocardiography (TEE or TOE) and computed tomography (CT) were 2 image-guided approaches that were used in this study. Full analysis set included all randomized subjects.

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

End point timeframe:

Baseline up to Day of first attempt of cardioversion procedure (Visit 2, up to 130 days)

| End point values | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 747 | | |
| Units: subjects | 383 | 399 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From baseline up to 30 days after cardioversion or 90 days after randomization, if cardioversion was not performed

Adverse event reporting additional description:

Same event may appear as adverse event (AE) and serious adverse event (SAE), what is presented are distinct events. Event may be categorized as serious in 1 subject and as non-serious in another subject or 1 subject may have experienced both serious and non-serious event during study. Safety data set included all treated subjects.

| | |
|---|---|
| Assessment type | Non-systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Apixaban |

Reporting group description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received Apixaban orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of Apixaban was based on investigator's judgement as per local label for the prevention of stroke and systemic embolism in subjects.

| | |
|---|---|
| Reporting group title | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) |

Reporting group description:

Subjects with non-valvular atrial fibrillation undergoing cardioversion, received parenteral heparin and/or oral Vitamin K antagonist as usual care, orally for 30 days after cardioversion or 90 days after randomization if cardioversion was not performed. The dosing of the parenteral heparin and Vitamin K antagonist was based on individual subject's sensitivity to the drug according to the investigators usual practice.

| **Serious adverse events** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 100 / 735 (13.61%) | 112 / 721 (15.53%) | |
| number of deaths (all causes) | 1 | 3 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ACUTE LEUKAEMIA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ADENOCARCINOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BREAST CANCER | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENDOMETRIAL CANCER | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| METASTASES TO BONE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PROSTATE CANCER | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SQUAMOUS CELL CARCINOMA OF SKIN | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| ARTERIAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ARTERIOVENOUS FISTULA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATOMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTENSION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTENSIVE CRISIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 2 / 721 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHEST PAIN | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HERNIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MUCOSAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MULTIPLE ORGAN DYSFUNCTION SYNDROME | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 3 / 735 (0.41%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| VAGINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE PULMONARY OEDEMA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATELECTASIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPNOEA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 735 (0.41%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EPISTAXIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MEDIASTINAL CYST | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MEDIASTINAL HAEMATOMA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMOTHORAX | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY CONGESTION | | | |
| subjects affected / exposed | 3 / 735 (0.41%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY HYPERTENSION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY OEDEMA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 2 / 721 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY SARCOIDOSIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| DEPRESSION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| COMPUTERISED TOMOGRAM CORONARY ARTERY ABNORMAL | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FUNCTIONAL RESIDUAL CAPACITY DECREASED | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERNATIONAL NORMALISED RATIO ABNORMAL | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| ARTERIAL BYPASS THROMBOSIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EYE INJURY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FALL | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEMUR FRACTURE | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEAD INJURY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OVERDOSE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 735 (0.00%) | 3 / 721 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RADIUS FRACTURE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TOXICITY TO VARIOUS AGENTS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRAUMATIC INTRACRANIAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VASCULAR PSEUDOANEURYSM | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| ADENOMATOUS POLYPOSIS COLI | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPERTROPHIC CARDIOMYOPATHY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ARTERIOSCLEROSIS CORONARY ARTERY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 27 / 735 (3.67%) | 40 / 721 (5.55%) | |
| occurrences causally related to treatment / all | 0 / 30 | 0 / 48 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL FLUTTER | | | |
| subjects affected / exposed | 3 / 735 (0.41%) | 6 / 721 (0.83%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL THROMBOSIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 3 / 721 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIOVENTRICULAR BLOCK COMPLETE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIOVENTRICULAR DISSOCIATION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRADYCARDIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 735 (0.68%) | 7 / 721 (0.97%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE ACUTE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE CONGESTIVE | | | |
| subjects affected / exposed | 9 / 735 (1.22%) | 7 / 721 (0.97%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIO-RESPIRATORY ARREST | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| CARDIOGENIC SHOCK | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONGESTIVE CARDIOMYOPATHY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CORONARY ARTERY DISEASE | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 6 / 721 (0.83%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CORONARY ARTERY STENOSIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ISCHAEMIC CARDIOMYOPATHY | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MITRAL VALVE INCOMPETENCE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MITRAL VALVE PROLAPSE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 3 / 721 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYOCARDIAL ISCHAEMIA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PALPITATIONS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERICARDITIS CONSTRICTIVE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SINUS ARREST | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SINUS NODE DYSFUNCTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 735 (0.27%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TACHYARRHYTHMIA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TACHYCARDIA INDUCED CARDIOMYOPATHY | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRICUSPID VALVE INCOMPETENCE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| BRAIN INJURY | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBRAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBRAL INFARCTION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CEREBROVASCULAR ACCIDENT | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 3 / 721 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEMENTIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIZZINESS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PRESYNCOPE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEIZURE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNCOPE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 2 / 721 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRANSIENT ISCHAEMIC ATTACK | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 2 / 721 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| HAEMORRHAGIC ANAEMIA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |

| | | | |
|---|---|---|---|
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DUODENAL ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ENTEROCOLITIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| FEMORAL HERNIA INCARCERATED | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRIC ULCER | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRITIS | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATOCHEZIA | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LARGE INTESTINE PERFORATION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| MELAENA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MESENTERIC PANNICULITIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OEDEMATOUS PANCREATITIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| OESOPHAGITIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PEPTIC ULCER | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PEPTIC ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HAEMORRHAGE | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SMALL INTESTINAL OBSTRUCTION | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| DRUG-INDUCED LIVER INJURY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEPATIC CONGESTION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| DECUBITUS ULCER | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIABETIC FOOT | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PETECHIAE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUBCUTANEOUS EMPHYSEMA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |

| | | | |
|---|---|---|---|
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 5 / 721 (0.69%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATURIA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POSTRENAL FAILURE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RENAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endocrine disorders | | | |
| ADRENAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TOXIC NODULAR GOITRE | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| FLANK PAIN | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| ABSCESS LIMB | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRONCHITIS | | | |
| subjects affected / exposed | 2 / 735 (0.27%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CELLULITIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ESCHERICHIA URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFECTION | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INFLUENZA | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTESTINAL SEPSIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUNG INFECTION | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 3 / 735 (0.41%) | 5 / 721 (0.69%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 0 / 721 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UROSEPSIS | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 1 / 735 (0.14%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 1 / 721 (0.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| **Non-serious adverse events** | Apixaban | Parenteral heparin/Oral Vitamin K Antagonist (Usual Care) | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 70 / 735 (9.52%) | 101 / 721 (14.01%) | |
| Investigations | | | |
| INTERNATIONAL NORMALISED RATIO ABNORMAL | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 19 / 721 (2.64%) | |
| occurrences (all) | 0 | 41 | |
| INTERNATIONAL NORMALISED RATIO INCREASED | | | |
| subjects affected / exposed | 0 / 735 (0.00%) | 27 / 721 (3.74%) | |
| occurrences (all) | 0 | 30 | |
| Cardiac disorders | | | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 43 / 735 (5.85%) | 46 / 721 (6.38%) | |
| occurrences (all) | 43 | 48 | |
| ATRIAL THROMBOSIS | | | |
| subjects affected / exposed | 17 / 735 (2.31%) | 13 / 721 (1.80%) | |
| occurrences (all) | 17 | 13 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 15 / 735 (2.04%) | 8 / 721 (1.11%) | |
| occurrences (all) | 15 | 8 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 22 February 2016 | Simultaneous treatment with both aspirin and a thienopyridine (eg, clopidogrel, ticlopidine, prasugrel) or simultaneous treatment with both aspirin and ticagrelor. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The prioritization of outcome measures is not mentioned in the study documents (Statistical Analysis Plan and Protocol). The prioritization of outcome measures is based on team's discretion.

Notes: