# Clinical trial results:
# Does Ticagrelor inhibit growth of small abdominal aortic aneurysms? A randomised controlled trial (TicAAA)

## Summary

| | |
|---|---|
| EudraCT number | 2013-002736-24 |
| Trial protocol | SE |
| Global end of trial date | 26 June 2017 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 27 October 2018 |
| First version publication date | 27 October 2018 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | TicAAA-1.0 |

**Additional study identifiers**

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

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Uppsala University Hospital |
| Sponsor organisation address | Akademiska sjukhuset ing 70, 1 tr, Uppsala, Sweden, |
| Public contact | Anders Wanhainen, Uppsala University Hospital, anders.wanhainen@surgsci.uu.se |
| Scientific contact | Anders Wanhainen, Uppsala University Hospital, anders.wanhainen@surgsci.uu.se |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 26 June 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 June 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 26 June 2017 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To investigate the efficacy of Ticagrelor on Abdominal aortic aneurysm (AAA)-expansion in a multi-centre, randomized, double-blinded for Ticagrelor and placebo.

Protection of trial subjects:

Patients were given full and adequate verbal and written information about the objectives, procedures and possible risks and benefits of the study, prior to enrolment. Study treatment was to be stopped in case of liver impairment, severe bleeding, elective aneurysm surgery, or the onset of any exclusion criteria. In the case of trauma during the study, the study drug was to be discontinued until the risk of bleeding ends.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 25 February 2014 |
| 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 | Sweden: 144 |
| Worldwide total number of subjects | 144 |
| EEA total number of subjects | 144 |

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) | 6 |
| From 65 to 84 years | 138 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

158 patients were enrolled in the study. Of these, there were 14 enrolment failures due to 7 patients who did not satisfy inclusion criteria #4 (documented AAA 35-49mm), 4 patients failing various exclusion criteria, and 3 patients who left by choice.

### Period 1

| | |
|---|---|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Blinding implementation details:

The active product and placebo were identical in appearance and packed in identical, non-transparent containers. Sealed envelopes with individual treatment codes showing allocated treatment for each randomised patient was kept by the PI, local pharmacy, and the Sponsor's safety department. The treatment code was not to be broken except in medical emergencies. Any breaking of the treatment code had to be documented.

### Arms

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

Arm description:

Ticagrelor 90 mg tablet twice daily for 12 months

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Ticagrelor |
| Investigational medicinal product code | SUB30898 |
| Other name | Brilique |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

90 mg tablet twice daily for 12 months

| | |
|---|---|
| **Arm title** | Placebo |

Arm description:

Ticagrelor placebo tablet twice daily for 12 months

| | |
|---|---|
| Arm type | Placebo |
| Investigational medicinal product name | Ticagrelor placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Ticagrelor placebo tablet twice daily for 12 months

| **Number of subjects in period 1** | Ticagrelor | Placebo |
|---|---|---|
| Started | 72 | 72 |
| Completed | 67 | 67 |
| Not completed | 5 | 5 |
| Adverse event, serious fatal | - | 2 |
| Physician decision | 1 | - |
| Elective aneurysm surgery | 1 | - |
| Adverse event, non-fatal | 3 | 1 |
| Protocol deviation | - | 2 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Ticagrelor |
| Reporting group description: | |
| Ticagrelor 90 mg tablet twice daily for 12 months | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Ticagrelor placebo tablet twice daily for 12 months | |

| Reporting group values | Ticagrelor | Placebo | Total |
|---|---|---|---|
| Number of subjects | 72 | 72 | 144 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 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) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 69.5 | 68.3 | |
| standard deviation | ± 4.6 | ± 4.2 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 4 | 2 | 6 |
| Male | 68 | 70 | 138 |
| Race | | | |
| Units: Subjects | | | |
| White | 71 | 70 | 141 |
| Other | 1 | 2 | 3 |
| Tobacco usage | | | |
| Smoking at enrollment was reported as never smoked, current smoker, or former smoker. | | | |
| Units: Subjects | | | |
| Current | 22 | 26 | 48 |
| Former | 40 | 39 | 79 |
| Never | 10 | 7 | 17 |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 86.3 | 88.1 | |
| standard deviation | ± 12.5 | ± 14.6 | - |
| Height | | | |
| Units: cm | | | |

| | | | |
|---|---|---|---|
| arithmetic mean | 177.6 | 179.4 | |
| standard deviation | ± 7.7 | ± 6.6 | - |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 27.39 | 27.31 | |
| standard deviation | ± 3.74 | ± 3.84 | - |

**Subject analysis sets**

| | |
|---|---|
| Subject analysis set title | Ticagrelor (PPA) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PPA population was pre-defined in the study protocol as patients with at least 80% compliance with the intended use, no major protocol deviations and with measure of primary efficacy endpoint at 12 months after randomisation.

| | |
|---|---|
| Subject analysis set title | Placebo (PPA) |
| Subject analysis set type | Per protocol |

Subject analysis set description:

The PPA population was pre-defined in the study protocol as patients with at least 80% compliance with the intended use, no major protocol deviations and with measure of primary efficacy endpoint at 12 months after randomisation.

| | |
|---|---|
| Subject analysis set title | Ticagrelor (ITT) |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The ITT population was pre-defined that patients with no post-dose observations for an efficacy endpoint should be removed from the ITT population.

| | |
|---|---|
| Subject analysis set title | Placebo (ITT) |
| Subject analysis set type | Intention-to-treat |

Subject analysis set description:

The ITT population was pre-defined that patients with no post-dose observations for an efficacy endpoint should be removed from the ITT population.

| **Reporting group values** | Ticagrelor (PPA) | Placebo (PPA) | Ticagrelor (ITT) |
|---|---|---|---|
| Number of subjects | 55 | 63 | 69 |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 69.4 | 68.7 | 69.5 |
| standard deviation | ± 4.5 | ± 4.2 | ± 4.5 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 2 | 4 |

| | | | |
|---|---|---|---|
| Male | 53 | 61 | 65 |

| | | | |
|---|---|---|---|
| Race<br>Units: Subjects | | | |
| White | 54 | 62 | 68 |
| Other | 1 | 1 | 1 |
| Tobacco usage | | | |
| Smoking at enrollment was reported as never smoked, current smoker, or former smoker. | | | |
| Units: Subjects | | | |
| Current | 13 | 23 | 21 |
| Former | 32 | 34 | 38 |
| Never | 10 | 6 | 10 |
| Weight<br>Units: kg | | | |
| arithmetic mean | 87.0 | 87.8 | 86.2 |
| standard deviation | ± 12.4 | ± 14.7 | ± 12.4 |
| Height<br>Units: cm | | | |
| arithmetic mean | 177.9 | 179.1 | 177.6 |
| standard deviation | ± 7.8 | ± 6.7 | ± 7.8 |
| BMI<br>Units: kg/m2 | | | |
| arithmetic mean | 27.51 | 27.32 | 27.33 |
| standard deviation | ± 3.79 | ± 3.88 | ± 3.75 |

| **Reporting group values** | Placebo (ITT) | | |
|---|---|---|---|
| Number of subjects | 70 | | |
| Age categorical<br>Units: Subjects | | | |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over | | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 68.3 | | |
| standard deviation | ± 4.2 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | | |
| Male | 68 | | |
| Race<br>Units: Subjects | | | |
| White | 68 | | |

| | | | |
|---|---|---|---|
| Other | 2 | | |
| Tobacco usage | | | |
| Smoking at enrollment was reported as never smoked, current smoker, or former smoker. | | | |
| Units: Subjects | | | |
| Current | 25 | | |
| Former | 39 | | |
| Never | 6 | | |
| Weight | | | |
| Units: kg | | | |
| arithmetic mean | 88.2 | | |
| standard deviation | ± 14.8 | | |
| Height | | | |
| Units: cm | | | |
| arithmetic mean | 179.3 | | |
| standard deviation | ± 6.6 | | |
| BMI | | | |
| Units: kg/m2 | | | |
| arithmetic mean | 27.38 | | |
| standard deviation | ± 3.88 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Ticagrelor |
| Reporting group description: | |
| Ticagrelor 90 mg tablet twice daily for 12 months | |
| Reporting group title | Placebo |
| Reporting group description: | |
| Ticagrelor placebo tablet twice daily for 12 months | |
| Subject analysis set title | Ticagrelor (PPA) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| The PPA population was pre-defined in the study protocol as patients with at least 80% compliance with the intended use, no major protocol deviations and with measure of primary efficacy endpoint at 12 months after randomisation. | |
| Subject analysis set title | Placebo (PPA) |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| The PPA population was pre-defined in the study protocol as patients with at least 80% compliance with the intended use, no major protocol deviations and with measure of primary efficacy endpoint at 12 months after randomisation. | |
| Subject analysis set title | Ticagrelor (ITT) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| The ITT population was pre-defined that patients with no post-dose observations for an efficacy endpoint should be removed from the ITT population. | |
| Subject analysis set title | Placebo (ITT) |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| The ITT population was pre-defined that patients with no post-dose observations for an efficacy endpoint should be removed from the ITT population. | |

### Primary: Difference in log-transformed volume of Abdominal Aortic Aneurysm (AAA) determined by magnetic resonance imaging (MRI) at 12 months

| | |
|---|---|
| End point title | Difference in log-transformed volume of Abdominal Aortic Aneurysm (AAA) determined by magnetic resonance imaging (MRI) at 12 months |
| End point description: | |
| The analysis performed on the ITT population was an Analysis of Covariance (ANCOVA) model with difference in log-transformed AAA volume at 12 month - baseline as response variable. Treatment (Ticagrelor vs. Placebo) was included as a fixed factor in the ANCOVA model and log-transformed baseline AAA volume was included as a covariate. Missing outcomes were imputed using last-value-carried-forward (LVCF), excluding patients with no post-baseline measurement. The result were presented as the estimated geometric mean ratio Ticagrelor/Placebo, with 95% C.I. and two-sided p-value.<br><br>AAA volume increase was similar in both arms, and there was no indication of a systemic difference between the treatments. The results of the secondary outcomes were in line with the primary variable. | |
| End point type | Primary |
| End point timeframe: | |
| Mean 12 months AAA volume increase from baseline (6 month values carried forward) | |

| End point values | Ticagrelor (ITT) | Placebo (ITT) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 67 | 69 | | |
| Units: cm3 | | | | |
| geometric mean (confidence interval 95%) | 1.091 (1.074 to 1.109) | 1.075 (1.061 to 1.090) | | |

## Statistical analyses

| Statistical analysis title | Analysis of difference in AAA volume by MRI |
|---|---|

Statistical analysis description:

The primary outcome was baseline-adjusted AAA volume at 12 months in the ITT population analysed using an ANCOVA model with difference in log-transformed AAA volume at 12 month - baseline as response variable. Treatment (Ticagrelor vs. Placebo) was included as a fixed factor in the ANCOVA model and log-transformed baseline AAA volume was included as a covariate.

| Comparison groups | Placebo (ITT) v Ticagrelor (ITT) |
|---|---|
| Number of subjects included in analysis | 136 |
| Analysis specification | Pre-specified |
| Analysis type | superiority[1] |
| P-value | = 0.205 |
| Method | ANCOVA |

Notes:

[1] - Missing outcomes were imputed using last-value-carried-forward (LVCF), excluding patients with no post-baseline measurement.

## Secondary: Difference in AAA diameter determined by MRI at 12 months vs at baseline

| End point title | Difference in AAA diameter determined by MRI at 12 months vs at baseline |
|---|---|

End point description:

67 Ticagrelor patients and 69 placebo patients were included in the ITT analysis, of which data for 2 Ticagrelor and 3 placebo patients were imputed using the 6-months value. Mean 12 months AAA diameter increase from baseline was 0.24 cm in the Ticagrelor treatment group and 0.18 cm in the placebo group, not affected by imputation.

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

End point timeframe:

Mean 12 months AAA diameter increase from baseline (6 month values carried forward) determined by magnetic resonance imaging (MRI)

| End point values | Ticagrelor (ITT) | Placebo (ITT) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 67[2] | 69[3] | | |
| Units: cm | | | | |
| arithmetic mean (confidence interval 95%) | 0.244 (0.190 to 0.298) | 0.185 (0.142 to 0.227) | | |

Notes:

[2] - 67 Ticagrelor patients were included, of which data for 2 were imputed using the 6-months value.

[3] - 69 Placebo patients were included, of which data for 3 were imputed using the 6-months value.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Difference in AAA diameter determined by ultrasound (US) at 12 months vs at baseline

| End point title | Difference in AAA diameter determined by ultrasound (US) at 12 months vs at baseline |
|---|---|

End point description:

69 Ticagrelor patients and 70 placebo patients were included in the ITT analysis, of which data for 2 Ticagrelor and 3 placebo patients were imputed using the 6-months value. Mean 12 months AAA diameter increase from baseline was 2.3 mm in the Ticagrelor treatment group and 2.2 mm in the placebo group, not affected by imputation.

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

End point timeframe:

Mean 12 months AAA diameter increase from baseline (6 month values carried forward) determined by ultrasound (US)

| **End point values** | Ticagrelor (ITT) | Placebo (ITT) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 69[4] | 70[5] | | |
| Units: mm | | | | |
| arithmetic mean (confidence interval 95%) | 2.29 (1.68 to 2.90) | 2.17 (1.65 to 2.70) | | |

Notes:

[4] - 69 Ticagrelor patients were included, of which 2 patients were imputed using the 6-months value.

[5] - 70 Placebo patients were included, of which 3 patients were imputed using the 6-months value.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Difference in thrombus volume determined by MRI at 12 months vs at baseline

| End point title | Difference in thrombus volume determined by MRI at 12 months vs at baseline |
|---|---|

End point description:

67 Ticagrelor patients and 69 placebo patients were included in the ITT analysis, of which data for 2 Ticagrelor and 3 placebo patients were imputed using the 6-months value.

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

End point timeframe:

Mean 12 months thrombus volume increase from baseline (6 month values carried forward) determined by MRI

| End point values | Ticagrelor (ITT) | Placebo (ITT) | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 67[6] | 69[7] | | |
| Units: cm3 | | | | |
| geometric mean (confidence interval 95%) | 1.130 (1.075 to 1.187) | 1.109 (1.066 to 1.155) | | |

Notes:

[6] - 67 Ticagrelor patients were included, of which 2 patients were imputed using the 6-months value.

[7] - 69 Placebo patients were included, of which 3 patients were imputed using the 6-months value.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Difference in need for surgery (≥ 55 mm) after 12 months

| End point title | Difference in need for surgery (≥ 55 mm) after 12 months |
|---|---|

End point description:

Need for surgery defined as aortic diameter 55 mm or larger, or reported need for surgery at 6 or 12 months ultrasound, or withdrawal from study due to need for surgery is presented for the ITT and PPA populations at 12 months.

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

End point timeframe:

Difference in need for surgery (≥ 55 mm) after 12 months

| End point values | Ticagrelor (PPA) | Placebo (PPA) | Ticagrelor (ITT) | Placebo (ITT) |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 55 | 63 | 69 | 70 |
| Units: Number of subjects | 2 | 0 | 4 | 0 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Difference in aneurysm rupture after 12 months

| End point title | Difference in aneurysm rupture after 12 months |
|---|---|

End point description:

Aneurysm rupture was recorded in the US CRF. In case an aneurysm rupture was detected as an AE it was added to the CRF-reported events. Patients that withdrew from follow-up without having an event were counted as no event. There were no aneurysm ruptures recorded in the study.

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

End point timeframe:

Difference in aneurysm rupture after 12 months

| End point values | Ticagrelor (PPA) | Placebo (PPA) | Ticagrelor (ITT) | Placebo (ITT) |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 55 | 63 | 69 | 70 |
| Units: Number of subjects | 0 | 0 | 0 | 0 |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

SAEs were recorded from the enrolment visit (visit 1) and SAEs/AEs were recorded from the baseline visit (visit 2) until the last visit (12 months after the baseline visit).

Adverse event reporting additional description:

SAEs were continuously recorded in the eCRF from visit 1 and SAE+AE were recorded from visit 2. All included patients were informed to contact the site if they experienced any more than normal bleeding and/or any liver impairment during the study.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | ICD-10 |
| Dictionary version | 2016 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Ticagrelor |

Reporting group description:

Ticagrelor 90 mg tablet twice daily for 12 months

| | |
|---|---|
| Reporting group title | Placebo |

Reporting group description:

Ticagrelor placebo tablet twice daily

| Serious adverse events | Ticagrelor | Placebo | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 72 (6.94%) | 7 / 72 (9.72%) | |
| number of deaths (all causes) | 0 | 2 | |
| number of deaths resulting from adverse events | 0 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Neoplasm | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Fracture of clavicle | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture of other parts of lower leg | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Acute vascular disorders of intestine | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac arrest, unspecified | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 2 / 72 (2.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Atrial fibrillation and atrial flutter, unspecified | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bradycardia, unspecified | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Surgical and medical procedures | | | |
| Other and unspecified medical devices associated with adverse incidents | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Haemorrhage, not elsewhere classified | | | |
| subjects affected / exposed | 2 / 72 (2.78%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascites | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Headache | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain, not elsewhere classified | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope and collapse | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Shock, unspecified | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| 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 | | | |
| Other specified disorders of male genital organs | | | |
| subjects affected / exposed | 1 / 72 (1.39%) | 0 / 72 (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 | | | |
| Paraesthesia of skin | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Depressive episode, unspecified | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Retention of urine | | | |
| subjects affected / exposed | 0 / 72 (0.00%) | 1 / 72 (1.39%) | |
| 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: 5 %

| **Non-serious adverse events** | Ticagrelor | Placebo | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 57 / 72 (79.17%) | 38 / 72 (52.78%) | |
| General disorders and administration site conditions | | | |
| Haemorrhage, not elsewhere classified | | | |
| subjects affected / exposed | 22 / 72 (30.56%) | 8 / 72 (11.11%) | |
| occurrences (all) | 33 | 11 | |
| Dyspnoea | | | |
| subjects affected / exposed | 19 / 72 (26.39%) | 4 / 72 (5.56%) | |
| occurrences (all) | 19 | 4 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute nasopharyngitis | | | |
| subjects affected / exposed | 4 / 72 (5.56%) | 2 / 72 (2.78%) | |
| occurrences (all) | 4 | 3 | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported