



Clinical trial results:

A 30 day international, randomized, parallel-group, double-blind, placebo-controlled phase IV study to evaluate efficacy and safety of pre-hospital vs. in-hospital initiation of ticagrelor therapy in STEMI patients planned for PCI

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2011-000214-19 |
| Trial protocol | GB DE AT SE DK NL ES IT HU |
| Global end of trial date | 14 November 2013 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 04 March 2016 |
| First version publication date | 04 March 2016 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D5130L00006 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01347580 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca |
| Sponsor organisation address | KC449/07 Pepparedsleden, Mölndal, Sweden, |
| Public contact | Dr Tomas Andersson MD, AstraZeneca, 46 8 553 260 00, |
| Scientific contact | Dr Tomas Andersson MD, AstraZeneca, tomas.lg.andersson@astrazeneca.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 | 23 April 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 November 2013 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of pre-hospital vs. in-hospital initiation of ticagrelor therapy by comparing the percentage of patients reaching the co-primary endpoint of TIMI flow grade 3 of MI culprit vessel at initial angiography or a $\geq 70\%$ ST-segment elevation resolution pre-PCI.

Protection of trial subjects:

Data Safety Monitoring Board

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 12 September 2011 |
| 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 | Australia: 43 |
| Country: Number of subjects enrolled | Austria: 42 |
| Country: Number of subjects enrolled | Algeria: 36 |
| Country: Number of subjects enrolled | Canada: 112 |
| Country: Number of subjects enrolled | Denmark: 75 |
| Country: Number of subjects enrolled | France: 660 |
| Country: Number of subjects enrolled | Germany: 98 |
| Country: Number of subjects enrolled | Hungary: 52 |
| Country: Number of subjects enrolled | Italy: 83 |
| Country: Number of subjects enrolled | Netherlands: 148 |
| Country: Number of subjects enrolled | Spain: 131 |
| Country: Number of subjects enrolled | Sweden: 202 |
| Country: Number of subjects enrolled | United Kingdom: 180 |
| Worldwide total number of subjects | 1862 |
| EEA total number of subjects | 1671 |

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) | 1179 |
| From 65 to 84 years | 683 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Patients were randomized in pre-hospital settings at 102 Emergency Medical Services between September 2011 and October 2013. 1875 patients were recruited in the study, 1862 consented patients were randomized.

Pre-assignment

Screening details:

no screening period

Period 1

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

Arms

| | |
|------------------------------|-------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Pre-hospital Ticagrelor |

Arm description:

Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

| | |
|--|------------------------------|
| Arm type | time administration strategy |
| Investigational medicinal product name | Ticagrelor |
| Investigational medicinal product code | AZD6140 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

loading dose of ticagrelor (180mg) followed by matching placebo. After the loading dose the patient will receive ticagrelor (90 mg bid) for 30 days

| | |
|------------------|------------------------|
| Arm title | In-hospital Ticagrelor |
|------------------|------------------------|

Arm description:

Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

| | |
|--|------------------------------|
| Arm type | time administration strategy |
| Investigational medicinal product name | Ticagrelor |
| Investigational medicinal product code | AZD6140 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

placebo followed by a loading dose of ticagrelor (180 mg).After the loading dose the patient will receive ticagrelor (90 mg bid) for 30 days.

| Number of subjects in period 1 | Pre-hospital Ticagrelor | In-hospital Ticagrelor |
|---------------------------------------|----------------------------|---------------------------|
| Started | 909 | 953 |
| Baseline period | 909 | 953 |
| Modified Intent to Treat population | 906 | 952 |
| Safety population | 908 | 950 |
| Completed | 844 | 897 |
| Not completed | 65 | 56 |
| Adverse event, serious fatal | 30 | 19 |
| Consent withdrawn by subject | 13 | 23 |
| Had other reason | 9 | 6 |
| Lost to follow-up | 3 | 1 |
| Protocol deviation | 10 | 7 |

Baseline characteristics

Reporting groups

| | |
|---|-------------------------|
| Reporting group title | Pre-hospital Ticagrelor |
| Reporting group description: Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days. | |
| Reporting group title | In-hospital Ticagrelor |
| Reporting group description: Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days. | |

| Reporting group values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | Total |
|--|-------------------------|------------------------|-------|
| Number of subjects | 909 | 953 | 1862 |
| Age categorical | | | |
| less than 65 years , 65 years and more | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 583 | 596 | 1179 |
| 65 years and over | 326 | 357 | 683 |
| Age Continuous Years | | | |
| Units: years | | | |
| arithmetic mean | 60.6 | 61 | |
| standard deviation | ± 12.38 | ± 12.49 | - |
| Gender, Male/Female | | | |
| Units: participants | | | |
| Female | 173 | 196 | 369 |
| Male | 736 | 757 | 1493 |
| Diabetes mellitus | | | |
| Units: Subjects | | | |
| yes | 115 | 138 | 253 |
| no/unknown | 794 | 815 | 1609 |
| Thrombolysis in Myocardial Infarction (TIMI) risk score | | | |
| TIMI risk is a score based on independent predictors of mortality such as age, diabetes mellitus, history of hypertension, history of angina, ST segment elevation. | | | |
| Units: Subjects | | | |
| 0-2 | 552 | 573 | 1125 |
| 3-6 | 337 | 365 | 702 |
| >6 | 20 | 15 | 35 |
| KILLIP CLASS | | | |
| Killip class assesses the presence and severity of heart failure by physical examination. Class I :No rales, no 3rd heart sound. Class 2: Rales in <1/2 lung field or presence of a 3rd heart sound. Class 3: Rales in >1/2 lung field–pulmonary edema. Class 4 : Cardiogenic shock–determined clinically. | | | |
| Units: Subjects | | | |
| I | 819 | 862 | 1681 |
| II, III, IV | 51 | 43 | 94 |
| unknown | 39 | 48 | 87 |
| Location of 1st medical contact | | | |
| Units: Subjects | | | |

| | | | |
|---|----------|----------|------|
| in ambulance | 689 | 723 | 1412 |
| in emergency department | 220 | 230 | 450 |
| Percutaneous coronary intervention (PCI) | | | |
| PCI is a non-surgery intervention performed to open blocked coronary arteries and to restore arterial blood flow to the heart tissue. | | | |
| Units: Subjects | | | |
| yes | 800 | 830 | 1630 |
| no | 109 | 123 | 232 |
| Any stents during PCI | | | |
| on patients with PCI | | | |
| Units: Subjects | | | |
| with stent | 760 | 776 | 1536 |
| without stent | 40 | 54 | 94 |
| no PCI | 109 | 123 | 232 |
| Time between the 2 loading doses | | | |
| Units: minutes | | | |
| median | 32 | 30 | |
| inter-quartile range (Q1-Q3) | 22 to 45 | 22 to 43 | - |

End points

End points reporting groups

| | |
|---|-------------------------|
| Reporting group title | Pre-hospital Ticagrelor |
| Reporting group description: | |
| Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days. | |
| Reporting group title | In-hospital Ticagrelor |
| Reporting group description: | |
| Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days. | |

Primary: TIMI flow grade 3 of MI culprit vessel (co-primary endpoint)

| | |
|---|--|
| End point title | TIMI flow grade 3 of MI culprit vessel (co-primary endpoint) |
| End point description: | |
| Thrombolysis In Myocardial Infarction (TIMI) flow grade classification is used to assess coronary blood flow in acute coronary syndromes. grade 0: no reperfusion, grade 1: penetration without perfusion, grade 2: Partial reperfusion, grade 3: complete perfusion. | |
| End point type | Primary |
| End point timeframe: | |
| At initial angiography, pre PCI | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 824 | 856 | | |
| Units: patients | 143 | 145 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | TIMI Flow grade 3 pre PCI |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1680 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.8214 ^[1] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.799 |
| upper limit | 1.327 |

Notes:

[1] - pvalue at 0.025 , adjusted for multiple comparisons

Primary: ST-segment elevation resolution pre PCI $\geq 70\%$ (co-primary endpoint)

| | |
|-----------------|---|
| End point title | ST-segment elevation resolution pre PCI $\geq 70\%$ (co-primary endpoint) |
|-----------------|---|

End point description:

ST segment elevation resolution is the mean ST elevation pre-hospital minus the mean ST elevation pre-PCI divided by the mean ST elevation pre-hospital. It is expressed as a percentage and split in 2 categories , complete ($\geq 70\%$) versus incomplete ($< 70\%$) resolution.

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

End point timeframe:

Between baseline and PCI

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 774 | 824 | | |
| Units: patients | 102 | 102 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | ST segment Elevation Resolution pre-PCI $\geq 70\%$ |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1598 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.6322 [2] |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.074 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.801 |
| upper limit | 1.441 |

Notes:

[2] - P value at 0.025 adjusted for multiple comparisons

Secondary: 1st Composite clinical endpoint

| | |
|-----------------|---------------------------------|
| End point title | 1st Composite clinical endpoint |
|-----------------|---------------------------------|

End point description:

death/MI/stroke/urgent revascularization/stent thrombosis. Adjudicated events except death

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

End point timeframe:

during the 30 days of treatment

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 906 | 952 | | |
| Units: patients | 41 | 42 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | first composite endpoint |
| Statistical analysis description: death, MI, stroke, urgent revascularisation, stent thrombosis. | |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1858 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.9056 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.027 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.661 |
| upper limit | 1.595 |

Secondary: 2nd composite clinical endpoint

| | |
|--|---------------------------------|
| End point title | 2nd composite clinical endpoint |
| End point description: Death/MI/urgent revascularization. Adjudicated events except death | |
| End point type | Secondary |
| End point timeframe: within 30 days of study | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 906 | 952 | | |
| Units: patients | 39 | 34 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | second composite clinical endpoint |
| Statistical analysis description: death, MI, urgent revascularisation. adjudicated event except deaths | |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1858 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.4168 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.215 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.942 |

Secondary: Definite stent thrombosis

| | |
|---|---------------------------|
| End point title | Definite stent thrombosis |
| End point description: Definite stent thrombosis is considered to have occurred by either angiographic or pathologic confirmation. It is an adjudicated endpoint | |
| End point type | Secondary |
| End point timeframe: during 30 days of treatment | |

| | | | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 906 | 952 | | |
| Units: patients | 2 | 11 | | |

Statistical analyses

| | |
|-----------------------------------|---------------------------|
| Statistical analysis title | definite stent thrombosis |
|-----------------------------------|---------------------------|

Statistical analysis description:

adjudicated endpoint, within 30 days of study

| | |
|---|--|
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1858 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0307 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.189 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.042 |
| upper limit | 0.856 |

Secondary: TIMI flow grade 3 post -PCI

| | |
|--|-----------------------------|
| End point title | TIMI flow grade 3 post -PCI |
| End point description: | |
| TIMI) flow grade 3 is complete perfusion post-PCI. | |
| End point type | Secondary |
| End point timeframe: | |
| at coroangiography post-PCI | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 760 | 784 | | |
| Units: patients | 625 | 630 | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | TIMI flow grade 3 post PCI |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1544 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.344 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.132 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.876 |
| upper limit | 1.462 |

Secondary: ST segment elevation resolution post-PCI \geq 70%

| | |
|---|---|
| End point title | ST segment elevation resolution post-PCI \geq 70% |
| End point description: ST segment elevation resolution post PCI \geq 70% is defined as complete resolution | |
| End point type | Secondary |
| End point timeframe: Between baseline and ECG 60 mn post-PCI | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 713 | 743 | | |
| Units: patients | 410 | 390 | | |

Statistical analyses

| | |
|---|---|
| Statistical analysis title | ST segment elevation resolution post-PCI \geq 70% |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1456 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.0547 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 1.225 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.996 |
| upper limit | 1.506 |

Secondary: Thrombotic bail-out with GPIIb/IIIa inhibitors at initial PCI

| | |
|--|---|
| End point title | Thrombotic bail-out with GPIIb/IIIa inhibitors at initial PCI |
| End point description: Glycoprotein (GP) IIb/IIIa inhibitors are often used as a rescue or bailout therapy to manage complications arising during percutaneous coronary intervention. | |

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: during PCI | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 906 | 952 | | |
| Units: patients | 78 | 100 | | |

Statistical analyses

| Statistical analysis title | Thrombotic bail-out |
|--|--|
| Statistical analysis description: with GPIIb/IIIa inhibitors at initial PCI | |
| Comparison groups | Pre-hospital Ticagrelor v In-hospital Ticagrelor |
| Number of subjects included in analysis | 1858 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.166 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 0.803 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.588 |
| upper limit | 1.096 |

Secondary: Major Bleeds within 48 hours

| | |
|---|------------------------------|
| End point title | Major Bleeds within 48 hours |
| End point description: non CABG related bleeds, (PLATO definition) include Life threatening and other major bleeds | |
| End point type | Secondary |
| End point timeframe: within 48 hours of first dose | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 950 | | |
| Units: patients | 16 | 15 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Minor and Major bleedings within 48 hours

| | |
|--|---|
| End point title | Minor and Major bleedings within 48 hours |
| End point description: non CABG related bleeds (PLATO definition) | |
| End point type | Secondary |
| End point timeframe: within 48 hours of first dose | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 950 | | |
| Units: patients | 24 | 24 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Major Bleeds after 48 hours

| | |
|---|-----------------------------|
| End point title | Major Bleeds after 48 hours |
| End point description: non CABG related bleeds (PLATO definition) include life threatening and other major bleedings | |
| End point type | Secondary |
| End point timeframe: after 48hours post-first dose | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 950 | | |
| Units: patients | 11 | 11 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Minor and Major bleeds after 48 hours

| | |
|--|---------------------------------------|
| End point title | Minor and Major bleeds after 48 hours |
| End point description: non CABG related bleeds (PLATO definition) | |
| End point type | Secondary |
| End point timeframe: after 48 hours post first dose | |

| End point values | Pre-hospital Ticagrelor | In-hospital Ticagrelor | | |
|-----------------------------|----------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 908 | 950 | | |
| Units: patients | 18 | 16 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

within 30 days of study

Adverse event reporting additional description:

Actual Treatment Safety analysis set concerns 1858 patients -

Ticagrelor pre-hosp:908 and Ticagrelor in-hosp: 950.

4 patients received study medication not according to randomization assignment

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------|
| Reporting group title | Ticagrelor Pre-Hosp |
|-----------------------|---------------------|

Reporting group description:

Loading dose of Ticagrelor (180 mg) followed by matching placebo. After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

| | |
|-----------------------|--------------------|
| Reporting group title | Ticagrelor In-Hosp |
|-----------------------|--------------------|

Reporting group description:

Placebo followed by a loading dose of Ticagrelor (180 mg). After the loading dose the patient will receive Ticagrelor (90 mg bid) for 30 days.

| Serious adverse events | Ticagrelor Pre-Hosp | Ticagrelor In-Hosp | |
|---|---------------------|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 140 / 908 (15.42%) | 143 / 950 (15.05%) | |
| number of deaths (all causes) | 30 | 19 | |
| number of deaths resulting from adverse events | 1 | 3 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ADRENAL ADENOMA | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BLADDER NEOPLASM | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC MYXOMA | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA (MALT TYPE) | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL NEOPLASM | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RENAL CANCER METASTATIC | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| AORTIC DISSECTION | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ARTERY DISSECTION | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATOMA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMODYNAMIC INSTABILITY | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| HYPERTENSION | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HYPOTENSION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| THROMBOPHLEBITIS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ORTHOSTATIC HYPOTENSION | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| 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 | | | |
| ASTHENIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC DEATH | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| CHEST PAIN | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 4 / 950 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DEVICE MALFUNCTION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MULTI-ORGAN FAILURE | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 4 / 908 (0.44%) | 5 / 950 (0.53%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUDDEN CARDIAC DEATH | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| SUDDEN DEATH | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 1 | |
| THROMBOSIS IN DEVICE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VESSEL PUNCTURE SITE HAEMATOMA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| ACUTE PULMONARY OEDEMA | | | |
| subjects affected / exposed | 3 / 908 (0.33%) | 3 / 950 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| ACUTE RESPIRATORY DISTRESS SYNDROME | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| ATELECTASIS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHRONIC OBSTRUCTIVE PULMONARY DISEASE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIAPHRAGMATIC PARALYSIS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSPNOEA | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| HAEMOTHORAX | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| LUNG DISORDER | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY EMBOLISM | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PULMONARY OEDEMA | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 4 / 908 (0.44%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RESPIRATORY FAILURE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CONFUSIONAL STATE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUICIDE ATTEMPT | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| HAEMOGLOBIN DECREASED | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEPATIC ENZYME INCREASED | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| NUTRITIONAL CONDITION | | | |

| | | | |
|---|-----------------|-----------------|--|
| ABNORMAL | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TROPONIN INCREASED | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| FEMORAL NECK FRACTURE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POST PROCEDURAL HAEMATOMA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| POST PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PROCEDURAL HAEMORRHAGE | | | |
| subjects affected / exposed | 3 / 908 (0.33%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SUBDURAL HAEMATOMA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| TRAUMATIC HAEMATOMA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UPPER LIMB FRACTURE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VASCULAR PSEUDOANEURYSM | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| 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 | | | |
| VENTRICULAR SEPTAL DEFECT | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cardiac disorders | | | |
| ACUTE MYOCARDIAL INFARCTION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| ANGINA PECTORIS | | | |
| subjects affected / exposed | 3 / 908 (0.33%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ANGINA UNSTABLE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| AORTIC VALVE INCOMPETENCE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|-----------------|--|
| ARRHYTHMIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| ARTERIOSPASM CORONARY | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIAL FIBRILLATION | | | |
| subjects affected / exposed | 4 / 908 (0.44%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| ATRIOVENTRICULAR BLOCK COMPLETE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 3 / 950 (0.32%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| BRADYCARDIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC ARREST | | | |
| subjects affected / exposed | 11 / 908 (1.21%) | 7 / 950 (0.74%) | |
| occurrences causally related to treatment / all | 0 / 11 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 5 | 0 / 1 | |
| CARDIAC ASTHMA | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 7 / 908 (0.77%) | 7 / 950 (0.74%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC FAILURE ACUTE | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIAC TAMPONADE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CARDIOGENIC SHOCK | | | |
| subjects affected / exposed | 17 / 908 (1.87%) | 16 / 950 (1.68%) | |
| occurrences causally related to treatment / all | 1 / 17 | 0 / 16 | |
| deaths causally related to treatment / all | 0 / 5 | 0 / 2 | |
| CARDIOPULMONARY FAILURE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| CONGESTIVE CARDIOMYOPATHY | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CORONARY ARTERY OCCLUSION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DRESSLER'S SYNDROME | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTERVENTRICULAR SEPTUM RUPTURE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| INTRACARDIAC THROMBUS | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 908 (0.22%) | 4 / 950 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LEFT VENTRICULAR DYSFUNCTION | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LEFT VENTRICULAR FAILURE | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MYOCARDIAL RUPTURE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 1 | |
| PALPITATIONS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 4 / 950 (0.42%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PERICARDITIS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TORSADE DE POINTES | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VENTRICLE RUPTURE | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 1 / 1 | |
| VENTRICULAR EXTRASYSTOLES | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| VENTRICULAR FIBRILLATION | | | |
| subjects affected / exposed | 23 / 908 (2.53%) | 30 / 950 (3.16%) | |
| occurrences causally related to treatment / all | 0 / 23 | 0 / 30 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| VENTRICULAR SEPTAL DEFECT ACQUIRED | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| VENTRICULAR TACHYCARDIA | | | |
| subjects affected / exposed | 6 / 908 (0.66%) | 7 / 950 (0.74%) | |
| occurrences causally related to treatment / all | 0 / 6 | 2 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| CEREBRAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 2 / 2 | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (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 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DYSARTHRIA | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMORRHAGE INTRACRANIAL | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HEMIPARESIS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LACUNAR INFARCTION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PRESYNCOPE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SYNCOPE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| TRANSIENT ISCHAEMIC ATTACK | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 3 / 950 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LEUKOCYTOSIS | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ear and labyrinth disorders | | | |
| VERTIGO | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN UPPER | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COLITIS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COLITIS ISCHAEMIC | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIARRHOEA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRIC ULCER | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRIC ULCER HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTRITIS | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROINTESTINAL TELANGIECTASIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATEMESIS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| HAEMATOCHEZIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| INTESTINAL ISCHAEMIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| MELAENA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RECTAL HAEMORRHAGE | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RETROPERITONEAL HAEMATOMA | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| BILIARY COLIC | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHOLECYSTITIS | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| CHOLECYSTITIS ACUTE | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| RASH PRURITIC | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| HAEMATURIA | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RENAL COLIC | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RENAL FAILURE | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 2 / 950 (0.21%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| RENAL FAILURE ACUTE | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 0 / 950 (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 | | | |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PAIN IN JAW | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PATHOLOGICAL FRACTURE | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (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 | | | |
| BILIARY SEPSIS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (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 | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| GASTROENTERITIS VIRAL | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| GROIN INFECTION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| LUNG INFECTION | | | |
| subjects affected / exposed | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| PNEUMONIA | | | |
| subjects affected / exposed | 2 / 908 (0.22%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| RELAPSING FEVER | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SEPSIS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (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 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| SKIN INFECTION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (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 | 0 / 908 (0.00%) | 1 / 950 (0.11%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| UROSEPSIS | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| DIABETES MELLITUS | | | |
| subjects affected / exposed | 1 / 908 (0.11%) | 0 / 950 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 3 %

| Non-serious adverse events | Ticagrelor Pre-Hosp | Ticagrelor In-Hosp | |
|---|---------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 469 / 908 (51.65%) | 529 / 950 (55.68%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 44 / 908 (4.85%) | 30 / 950 (3.16%) | |
| occurrences (all) | 45 | 32 | |
| Cardiac disorders | | | |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 79 / 908 (8.70%) | 81 / 950 (8.53%) | |
| occurrences (all) | 85 | 81 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 30 / 908 (3.30%) | 38 / 950 (4.00%) | |
| occurrences (all) | 32 | 39 | |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 32 / 908 (3.52%) | 37 / 950 (3.89%) | |
| occurrences (all) | 33 | 39 | |
| Cardiac failure | | | |
| subjects affected / exposed | 30 / 908 (3.30%) | 33 / 950 (3.47%) | |
| occurrences (all) | 30 | 35 | |
| Bradycardia | | | |

| | | | |
|--|--|--|--|
| subjects affected / exposed occurrences (all) | 28 / 908 (3.08%) 31 | 26 / 950 (2.74%) 28 | |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 19 / 908 (2.09%) 20 | 31 / 950 (3.26%) 33 | |
| General disorders and administration site conditions Non cardiac chest pain subjects affected / exposed occurrences (all) | 42 / 908 (4.63%) 47 | 52 / 950 (5.47%) 55 | |
| Gastrointestinal disorders Dyspnoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) | 62 / 908 (6.83%) 63 41 / 908 (4.52%) 42 34 / 908 (3.74%) 36 | 86 / 950 (9.05%) 87 49 / 950 (5.16%) 49 40 / 950 (4.21%) 40 | |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 28 / 908 (3.08%) 28 | 26 / 950 (2.74%) 26 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 22 June 2011 | To introduce an ECG sub-study to the ATLANTIC main study. This amendment was never implemented. |
| 19 December 2011 | To introduce the PRIVATE ATLANTIC sub-study to the main study. This was implemented in France and UK only. |

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.

This urgent setting study included 8.6% of patients with symptoms of MI in ambulance but having finally not a STEMI diagnosis in cathlab.
No prespecified hypothesis and procedure for adjustment was made on secondary endpoints.

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/25175921>