



## Clinical trial results:

### A Randomized, Open-Label, Multi-Center, Active-Controlled, Parallel Group Study to Determine the Efficacy and Safety of the REG1 Anticoagulation System Compared to Bivalirudin in Patients Undergoing Percutaneous Coronary Intervention

#### Summary

|                          |  |
|--------------------------|--|
| EudraCT number           | 2013-001384-23                               |
| Trial protocol           | HU EE DE NL PT AT GB IT BE SK ES DK PL CZ FR |
| Global end of trial date | 01 September 2014                            |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 23 August 2019 |
| First version publication date | 23 August 2019 |

#### Trial information

##### Trial identification

|                       |              |
|-----------------------|--------------|
| Sponsor protocol code | REG1-CLIN310 |
|-----------------------|--------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01848106 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Regado Biosciences, Inc   |
| Sponsor organisation address | Clonsaugh Business and Technology Park, Coolock, Dublin, Ireland, D17 E400                  |
| Public contact               | Clinical Trials Registry Team, Allergan plc, 001 8772778566, IR-CTRegistration@Allergan.com |
| Scientific contact           | Therapeutic Area Head, Allergan plc, 001 862-261-7000, IR-CTRegistration@Allergan.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:

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**Results analysis stage**

|  |                   |
|--|-------------------|
| Analysis stage                                       | Final             |
| Date of interim/final analysis                       | 29 June 2014      |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 01 September 2014 |
| Was the trial ended prematurely?                     | No                |

Notes:

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**General information about the trial**

Main objective of the trial:

The main objective of this trial was to determine the efficacy of REG1 compared to bivalirudin in participants with coronary artery disease (CAD) undergoing Percutaneous Coronary Intervention (PCI) for preventing the composite of death, nonfatal myocardial infarction, nonfatal stroke and urgent target lesion revascularization (TLR) through Day 3 post randomisation.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy:

All participants were to receive an initial dose of aspirin in addition to loading and maintenance doses of an ADP/P2Y12 inhibitor (dose and timing per local standard of care); administration of these medications prior to randomization and start of PCI.

Evidence for comparator: -

|   |                   |
|---|-------------------|
| Actual start date of recruitment                          | 13 September 2013 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | Yes               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |                     |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United States: 2253 |
| Country: Number of subjects enrolled | United Kingdom: 979 |
| Worldwide total number of subjects   | 3232                |
| EEA total number of subjects         | 979                 |

Notes:

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**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)                      | 1616 |

|                     |      |
|---------------------|------|
| From 65 to 84 years | 1616 |
| 85 years and over   | 0    |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

3232 participants were enrolled and randomised from 325 centres.

### Period 1

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

### Arms

|                              |                                  |
|------------------------------|----------------------------------|
| Are arms mutually exclusive? | Yes                              |
| <b>Arm title</b>             | Reg 1 (Pegnivacogin/Anivamersen) |

Arm description:

Pegnivacogin 1.0 mg/kg, intravenous (IV) bolus injection or arterial sheath prior to the PCI.  
Anivamersen 0.5 mg/kg (80% reversal), IV bolus injection after PCI.

|  |                          |
|--|--------------------------|
| Arm type                               | Experimental             |
| Investigational medicinal product name | Pegnivacogin/Anivamersen |
| Investigational medicinal product code |                          |
| Other name                             |                          |
| Pharmaceutical forms                   | Injection                |
| Routes of administration               | Intravenous use          |

Dosage and administration details:

Pegnivacogin 1.0 mg/kg, intravenous (IV) bolus injection or arterial sheath prior to the PCI.  
Anivamersen 0.5 mg/kg (80% reversal), IV bolus injection after PCI.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Bivalirudin |
|------------------|-------------|

Arm description:

Bivalirudin 0.75 mg/kg IV bolus injection or arterial sheath prior to PCI, immediately followed by an IV infusion of 1.75 mg/kg/hour until completion of PCI.

|  |                 |
|--|-----------------|
| Arm type                               | Experimental    |
| Investigational medicinal product name | Bivalirudin     |
| Investigational medicinal product code |                 |
| Other name                             |                 |
| Pharmaceutical forms                   | Injection       |
| Routes of administration               | Intravenous use |

Dosage and administration details:

Bivalirudin 0.75 mg/kg IV bolus injection or arterial sheath prior to PCI, immediately followed by an IV infusion of 1.75 mg/kg/hour until completion of PCI.

| Number of subjects in period 1 | Reg 1<br>(Pegnivacogin/Anivamersen) | Bivalirudin |
|--------------------------------|-------------------------------------|-------------|
|                                |                                     |             |
| Started                        | 1616                                | 1616        |
| Completed                      | 1613                                | 1608        |
| Not completed                  | 3                                   | 8           |
| Withdrew Consent               | -                                   | 2           |
| Unknown                        | -                                   | 1           |
| Unable to Contact              | 3                                   | 5           |

## Baseline characteristics

### Reporting groups

|  |                                  |
|--|----------------------------------|
| Reporting group title  | Reg 1 (Pegnivacogin/Anivamersen) |
| Reporting group description:<br>Pegnivacogin 1.0 mg/kg, intravenous (IV) bolus injection or arterial sheath prior to the PCI.<br>Anivamersen 0.5 mg/kg (80% reversal), IV bolus injection after PCI. |                                  |
| Reporting group title  | Bivalirudin                      |
| Reporting group description:<br>Bivalirudin 0.75 mg/kg IV bolus injection or arterial sheath prior to PCI, immediately followed by an IV infusion of 1.75 mg/kg/hour until completion of PCI.        |                                  |

| Reporting group values  | Reg 1<br>(Pegnivacogin/Anivamersen) | Bivalirudin     | Total |
|---|-------------------------------------|-----------------|-------|
| Number of subjects  | 1616                                | 1616            | 3232  |
| Age Categorical<br>Units: Subjects                                      |                                     |                 |       |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 65.4<br>± 10.68                     | 65.2<br>± 10.73 | -     |
| Gender Categorical<br>Units: Subjects                                   |                                     |                 |       |
| Female  | 401                                 | 432             | 833   |
| Male  | 1215                                | 1184            | 2399  |

## End points

### End points reporting groups

|   |                                  |
|---|----------------------------------|
| Reporting group title   | Reg 1 (Pegnivacogin/Anivamersen) |
| Reporting group description:<br>Pegnivacogin 1.0 mg/kg, intravenous (IV) bolus injection or arterial sheath prior to the PCI.<br>Anivamersen 0.5 mg/kg (80% reversal), IV bolus injection after PCI.  |                                  |
| Reporting group title   | Bivalirudin                      |
| Reporting group description:<br>Bivalirudin 0.75 mg/kg IV bolus injection or arterial sheath prior to PCI, immediately followed by an IV infusion of 1.75 mg/kg/hour until completion of PCI.   |                                  |
| Subject analysis set title  | Subgroup A                       |
| Subject analysis set type   | Sub-group analysis               |
| Subject analysis set description:<br>Subgroup A included participants who had acute coronary syndrome with positive cardiac biomarkers within the previous 7 days before enrollment.  |                                  |
| Subject analysis set title  | Subgroup B and C                 |
| Subject analysis set type   | Sub-group analysis               |
| Subject analysis set description:<br>Subgroup B included participants who had acute coronary syndrome with positive biomarkers more than 7 days before enrollment, had unstable angina without positive biomarkers, were older than 70 years, had diabetes or chronic kidney disease, had planned multivessel percutaneous coronary intervention, had undergone previous coronary artery bypass graft (CABG) surgery, or had peripheral vascular disease. Subgroup C included participants not meeting criteria for subgroups A or B. |                                  |

### Primary: Number of Participants With at Least 1 of the Composite Events of Death, Non-Fatal MI, Non-Fatal Stroke and UTLR Through Day 3 Post Randomization: CEC Adjudicated Data

|  |   |
|--|---|
| End point title  | Number of Participants With at Least 1 of the Composite Events of Death, Non-Fatal MI, Non-Fatal Stroke and UTLR Through Day 3 Post Randomization: CEC Adjudicated Data |
| End point description:<br>Clinical Events Committee (CEC) Adjudicated Data is provided for the composite of events of Death, Non-Fatal Myocardial Infarction (MI), Non-fatal Stroke and Urgent Target Lesion Revascularization (UTLR). Intent-to-treat (ITT) population included all randomised participants. Number analysed is the number of participants with complete follow up information through Day 3. |   |
| End point type   | Primary   |
| End point timeframe:<br>Baseline (Day 0 prior to PCI) to Day 3 post randomisation  |   |

| End point values            | Reg 1<br>(Pegnivacogin/<br>Anivamersen) | Bivalirudin     |  |  |
|-----------------------------|---|-----------------|--|--|
| Subject group type          | Reporting group                         | Reporting group |  |  |
| Number of subjects analysed | 1615                                    | 1613            |  |  |
| Units: participants         |   |                 |  |  |
| Death                       | 2                                       | 5               |  |  |
| MI                          | 103                                     | 93              |  |  |
| Stroke                      | 1                                       | 3               |  |  |
| Urgent TLR                  | 4                                       | 8               |  |  |

## Statistical analyses

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Death  |
| Comparison groups                       | Reg 1 (Pegnivacogin/Anivamersen) v Bivalirudin |
| Number of subjects included in analysis | 3228   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.2556                                       |
| Method                                  | Cochran-Mantel-Haenszel                        |
| Parameter estimate                      | Odds ratio (OR)                                |
| Point estimate                          | 0.4  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.08   |
| upper limit                             | 2.06   |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | MI   |
| Comparison groups                       | Reg 1 (Pegnivacogin/Anivamersen) v Bivalirudin |
| Number of subjects included in analysis | 3228   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.4673                                       |
| Method                                  | Cochran-Mantel-Haenszel                        |
| Parameter estimate                      | Odds ratio (OR)                                |
| Point estimate                          | 1.11   |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.83   |
| upper limit                             | 1.49   |

|                                   |  |
|-----------------------------------|--|
| <b>Statistical analysis title</b> | Stroke   |
| Comparison groups                 | Reg 1 (Pegnivacogin/Anivamersen) v Bivalirudin |



|   |                         |
|---|-------------------------|
| Number of subjects included in analysis | 3228                    |
| Analysis specification                  | Pre-specified           |
| Analysis type                           | superiority             |
| P-value                                 | = 0.3168                |
| Method                                  | Cochran-Mantel-Haenszel |
| Parameter estimate                      | Odds ratio (OR)         |
| Point estimate                          | 0.33                    |
| Confidence interval                     |                         |
| level                                   | 95 %                    |
| sides                                   | 2-sided                 |
| lower limit                             | 0.03                    |
| upper limit                             | 3.2                     |

|   |  |
|---|--|
| <b>Statistical analysis title</b>       | Urgent TLR                                     |
| Comparison groups                       | Reg 1 (Pegnivacogin/Anivamersen) v Bivalirudin |
| Number of subjects included in analysis | 3228   |
| Analysis specification                  | Pre-specified                                  |
| Analysis type                           | superiority                                    |
| P-value                                 | = 0.2466                                       |
| Method                                  | Cochran-Mantel-Haenszel                        |
| Parameter estimate                      | Odds ratio (OR)                                |
| Point estimate                          | 0.5  |
| Confidence interval                     |  |
| level                                   | 95 %   |
| sides                                   | 2-sided  |
| lower limit                             | 0.15   |
| upper limit                             | 1.66   |

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**Secondary: Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke, UTLR, and Stent Thrombosis (including Intraprocedural) through Day 3: CEC Adjudicated Data**

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|  |   |
|--|---|
| End point title  | Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke, UTLR, and Stent Thrombosis (including Intraprocedural) through Day 3: CEC Adjudicated Data |
| End point description:   |   |
| CEC Adjudicated Data is provided for the composite of events of Death, Non-Fatal MI, Non-fatal Stroke and UTLR and Stent Thrombosis. ITT population included all randomised participants. Number analysed is the number of participants with complete follow up information through Day 3. |   |
| End point type   | Secondary   |
| End point timeframe:   |   |
| Baseline (Day 0 prior to PCI) to Day 3 post randomisation  |   |

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| End point values            | Reg 1<br>(Pegnivacogin/<br>Anivamersen) | Bivalirudin     |  |  |
|-----------------------------|---|-----------------|--|--|
| Subject group type          | Reporting group                         | Reporting group |  |  |
| Number of subjects analysed | 1615                                    | 1613            |  |  |
| Units: participants         | 108                                     | 103             |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Major Non-Coronary Artery Bypass Graft (CABG) Bleeding [Bleeding Academic Research Consortium (BARC) Types 3 and 5] Through Day 3: CEC Adjudicated Data

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Major Non-Coronary Artery Bypass Graft (CABG) Bleeding [Bleeding Academic Research Consortium (BARC) Types 3 and 5] Through Day 3: CEC Adjudicated Data |
|-----------------|---|

End point description:

BARC criteria for bleeding include 5 types ranging from 1=bleeding is not actionable to 5=fatal bleeding. Type 3 bleeding: 3a=hemoglobin drop of 3 to 5 g/dL, transfusion of packed red blood cells or whole blood; 3b= hemoglobin drop  $\geq$  5 g/dL, cardiac tamponade, requiring surgical intervention, requiring intravenous vasoactive agents; 3c=intracranial hemorrhage, intraocular bleeding. Type 5 fatal bleeding: 5a=probable fatal clinically suspicious; 5 b=fatal confirmed by autopsy or imaging. Safety population included all participants who were randomised and received at least one dose of study drug. Number analysed is the number of participants with complete follow up information through Day 3.

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

End point timeframe:

Baseline (Day 0 prior to PCI) to Day 3 post randomisation

| End point values            | Reg 1<br>(Pegnivacogin/<br>Anivamersen) | Bivalirudin     |  |  |
|-----------------------------|---|-----------------|--|--|
| Subject group type          | Reporting group                         | Reporting group |  |  |
| Number of subjects analysed | 1603                                    | 1600            |  |  |
| Units: participants         | 7                                       | 2               |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal stroke, and UTLR through Day 30: CEC Adjudicated Data

|                 |  |
|-----------------|--|
| End point title | Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal stroke, and UTLR through Day 30: CEC Adjudicated Data |
|-----------------|--|

End point description:

CEC Adjudicated Data is provided for the composite of events of Death, Non-Fatal MI, Non-fatal Stroke

and UTLR and. ITT population included all randomised participants. Number analysed is the number of participants with complete follow up information through Day 30.

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

End point timeframe:

Baseline (Day 0 prior to PCI) to Day 30 post randomisation

| End point values            | Reg 1<br>(Pegnivacogin/<br>Anivamersen) | Bivalirudin     |  |  |
|-----------------------------|---|-----------------|--|--|
| Subject group type          | Reporting group                         | Reporting group |  |  |
| Number of subjects analysed | 1613                                    | 1608            |  |  |
| Units: participants         | 122                                     | 122             |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke, and UTLR through Day 3 in Subgroup A

|                 |   |
|-----------------|---|
| End point title | Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke, and UTLR through Day 3 in Subgroup A |
|-----------------|---|

End point description:

Subgroup A included participants with ischemic symptoms at rest and positive cardiac biomarkers (troponin I or T or creatine kinase-MB) related to an acute coronary syndrome (ACS) event.

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

End point timeframe:

Baseline (Day 0 prior to PCI) through Day 3 post randomisation

| End point values            | Subgroup A           |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 493                  |  |  |  |
| Units: participants         | 42                   |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke and UTLR through Day 3 in Subgroups B and C (Negative Cardiac Biomarkers)

|                 |   |
|-----------------|---|
| End point title | Number of Participants with at Least 1 of the Composite Events of Death, Non-fatal MI, Non-fatal Stroke and UTLR through Day 3 in Subgroups B and C (Negative Cardiac Biomarkers) |
|-----------------|---|

End point description:

Subgroups B and C participants not meeting criteria for Subgroup A.

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

End point timeframe:

Baseline (Day 0 prior to PCI) through Day 3 post randomisation

| End point values            | Subgroup B and C     |  |  |  |
|-----------------------------|----------------------|--|--|--|
| Subject group type          | Subject analysis set |  |  |  |
| Number of subjects analysed | 2739                 |  |  |  |
| Units: participants         | 169                  |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Participants with Major Non-CABG bleeding (BARC Types 3 and 5) through Day 30: CEC Adjudicated Data

|                 |   |
|-----------------|---|
| End point title | Number of Participants with Major Non-CABG bleeding (BARC Types 3 and 5) through Day 30: CEC Adjudicated Data |
|-----------------|---|

End point description:

BARC criteria for bleeding include 5 types ranging from 1=bleeding is not actionable to 5=fatal bleeding. Type 3 bleeding: 3a=hemoglobin drop of 3 to 5 g/dL, transfusion of packed red blood cells or whole blood; 3b= hemoglobin drop $\geq$ 5 g/dL, cardiac tamponade, requiring surgical intervention, requiring intravenous vasoactive agents; 3c=intracranial hemorrhage, Intraocular bleeding. Type 5 fatal bleeding: 5a=probable fatal clinically suspicious; 5 b=fatal confirmed by autopsy or imaging. Safety population included all participants who were randomised and received at least one dose of study drug.

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

End point timeframe:

Baseline (Day 0 prior to PCI) through Day 30 post randomisation

| End point values            | Reg 1 (Pegnivacogin/ Anivamersen) | Bivalirudin     |  |  |
|-----------------------------|-----------------------------------|-----------------|--|--|
| Subject group type          | Reporting group                   | Reporting group |  |  |
| Number of subjects analysed | 1601                              | 1596            |  |  |
| Units: participants         | 11                                | 4               |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

Randomisation through 3 days post-randomisation for Adverse Events (AEs) and Randomisation through 30 days post-randomisation for Serious Adverse Events (SAEs) [Up to Day 35]

Adverse event reporting additional description:

Events that met efficacy and bleeding endpoint criteria were not considered AEs or SAEs. In addition, pre-defined disease-related and procedural-related events were not considered AEs or SAEs.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

### Reporting groups

|                       |                                  |
|-----------------------|----------------------------------|
| Reporting group title | Reg 1 (Pegnivacogin/Anivamersen) |
|-----------------------|----------------------------------|

Reporting group description:

Pegnivacogin administered by a bolus injection of 1.0 mg/kg over approximately 2 minutes, IV or arterial sheath prior to the PCI procedure. Anivamersen was administered at 0.5 mg/kg (80% reversal), IV bolus injection over approximately 1 minute upon completion of the PCI procedure.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Bivalirudin |
|-----------------------|-------------|

Reporting group description:

Bivalirudin administered by a bolus injection of 0.75 mg/kg IV or arterial sheath prior to the PCI procedure, immediately followed by an IV infusion of 1.75 mg/kg/hour until completion of the procedure (infusion rate adjusted for renal insufficient participants per the local bivalirudin label).

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: There were no non-serious adverse events at the 5% frequency threshold for reporting.

| Serious adverse events  | Reg 1<br>(Pegnivacogin/Anivamersen) | Bivalirudin       |  |
|---|-------------------------------------|-------------------|--|
| Total subjects affected by serious adverse events                   |                                     |                   |  |
| subjects affected / exposed   | 29 / 1605 (1.81%)                   | 13 / 1601 (0.81%) |  |
| number of deaths (all causes)                                       | 8                                   | 12                |  |
| number of deaths resulting from adverse events                      | 1                                   | 0                 |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                                     |                   |  |
| Prostate cancer   |                                     |                   |  |
| subjects affected / exposed   | 1 / 1605 (0.06%)                    | 0 / 1601 (0.00%)  |  |
| occurrences causally related to treatment / all                     | 0 / 1                               | 0 / 0             |  |
| deaths causally related to treatment / all                          | 0 / 1                               | 0 / 0             |  |
| Injury, poisoning and procedural complications                      |                                     |                   |  |
| Post-traumatic pain   |                                     |                   |  |
| subjects affected / exposed   | 0 / 1605 (0.00%)                    | 1 / 1601 (0.06%)  |  |
| occurrences causally related to treatment / all                     | 0 / 0                               | 0 / 1             |  |
| deaths causally related to treatment / all                          | 0 / 0                               | 0 / 0             |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| Vascular disorders                              |                  |                  |  |
| Thrombophlebitis                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Nervous system disorders                        |                  |                  |  |
| Convulsion                                      |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Syncope   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (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 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Grand mal convulsion                            |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Headache  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Immune system disorders                         |                  |                  |  |
| Anaphylactic reaction                           |                  |                  |  |
| subjects affected / exposed                     | 6 / 1605 (0.37%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 5 / 6            | 0 / 1            |  |
| deaths causally related to treatment / all      | 1 / 1            | 0 / 0            |  |
| Hypersensitivity                                |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 4 / 1605 (0.25%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 3 / 4            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Eye disorders                                   |                  |                  |  |
| Eye pain  |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (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                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Duodenal ulcer                                  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Dyspepsia                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastrooesophageal reflux disease                |                  |                  |  |
| subjects affected / exposed                     | 2 / 1605 (0.12%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 2            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Colitis ischaemic                               |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastritis                                       |                  |                  |  |

|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (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 |                  |                  |  |
| Chronic obstructive pulmonary disease           |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Acute respiratory failure                       |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Pleural effusion                                |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Respiratory failure                             |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 1            | 0 / 0            |  |
| Hepatobiliary disorders                         |                  |                  |  |
| Biliary colic                                   |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Musculoskeletal and connective tissue disorders |                  |                  |  |
| Bursitis  |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gouty arthritis                                 |                  |                  |  |



|   |                  |                  |  |
|---|------------------|------------------|--|
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1            | 0 / 0            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| <b>Infections and infestations</b>              |                  |                  |  |
| Incision site infection                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Gastroenteritis                                 |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Bacteraemia                                     |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Pneumonia                                       |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 2 / 1601 (0.12%) |  |
| occurrences causally related to treatment / all | 0 / 1            | 0 / 2            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 1            |  |
| Thrombophlebitis septic                         |                  |                  |  |
| subjects affected / exposed                     | 0 / 1605 (0.00%) | 1 / 1601 (0.06%) |  |
| occurrences causally related to treatment / all | 0 / 0            | 0 / 1            |  |
| deaths causally related to treatment / all      | 0 / 0            | 0 / 0            |  |
| Tinea pedis                                     |                  |                  |  |
| subjects affected / exposed                     | 1 / 1605 (0.06%) | 0 / 1601 (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: 5 %

|  |                                     |                  |  |
|--|-------------------------------------|------------------|--|
| <b>Non-serious adverse events</b>  | Reg 1<br>(Pegnivacogin/Anivamersen) | Bivalirudin      |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed | 0 / 1605 (0.00%)                    | 0 / 1601 (0.00%) |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment   |
|-----------------|---|
| 22 January 2014 | The following changes were done as per Amendment 1:<br>Protocol amendment was done primarily in response to health authority feedback requesting stronger wording about males who could father a child during study participation and women who may be nursing during study participation. Stronger wording was added related to both of these special participant circumstances. Clarified 2 of the 8 possible risk factors used to define Subgroup B of participants – The risk factor, "Remote acute coronary syndrome (> 7 days) with positive cardiac biomarkers" was changed to "Current presentation with an acute coronary syndrome with positive biomarkers > 7 days prior to randomization." – The risk factor "Unstable angina (ACS without positive cardiac biomarkers)" became "Current presentation with unstable angina (ACS without positive cardiac biomarkers)." Changed the required time interval between randomization and any planned staged PCI procedure (post index PCI) so that staged PCI was excluded if planned within 30 days, rather than within 3 days, after randomization. Clarified that all participants were to receive dual antiplatelet therapy for the duration of the study; and clarified recommendations for the use of aspirin and ADP/P2Y12 inhibitors and the protocol restriction of GP IIb/IIIa inhibitors to only provisional use for procedural or angiographic complications. Clarified that "post dosing" window of time for laboratory testing referred to post bivalirudin bolus dose or post pegnivacogin dose, and not to anivamersen dose. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date         | Interruption   | Restart date |
|--------------|--|--------------|
| 29 June 2014 | The study was terminated for safety reasons on 29 June 2014 and was put on FDA clinical hold on 9 July 2014. | -            |

Notes:

### Limitations and caveats

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

In order to submit summary results, estimated data was entered in the Trial Information Age and Country fields. Due to acquisition, the sponsor does not have access to detailed demographic information. More information: (PubMed ID: 26547100).

Notes:

### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/26547100>