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	Clonshaugh 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:

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:

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:

Population of trial subjects

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:

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
Arm title	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.

Arm title	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 (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:	
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.	
Reporting group title	Bivalirudin
Reporting group 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.	

Reporting group values	Reg 1 (Pegnivacogin/Anivamersen)	Bivalirudin	Total
Number of subjects	1616	1616	3232
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	65.4	65.2	
standard deviation	± 10.68	± 10.73	-
Gender Categorical 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:	
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.	
Reporting group title	Bivalirudin
Reporting group 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.	
Subject analysis set title	Subgroup A
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
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:	
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:	
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:	
Baseline (Day 0 prior to PCI) to Day 3 post randomisation	

End point values	Reg 1 (Pegnivacogin/ 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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

Statistical analysis title	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

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

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

End point values	Reg 1 (Pegnivacogin/ 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>=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 (Pegnivacogin/ 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 (Pegnivacogin/ 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>=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[1]

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 (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	
Infections and infestations			
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 %

Non-serious adverse events	Reg 1 (Pegnivacogin/Anivamersen)	Bivalirudin	
Total subjects affected by non-serious adverse events 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: 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