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

Published: 10-10-2013
Last updated: 23-04-2024

Primary To determine the efficacy of REG1 compared to bivalirudin in patients with coronary artery disease (CAD) undergoing Percutaneous Coronary Intervention (PCI) for preventing the composite of death, nonfatal myocardial infarction, nonfatal...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON40245

Source
ToetsingOnline

Brief title
REG1-CLIN310

Condition

- Coronary artery disorders

Synonym
blockage in an artery, Heart disease

Research involving
Human

Sponsors and support

Primary sponsor: Regado Biosciences, Inc
Source(s) of monetary or material Support: Regado Biosciences;Inc

Intervention

Keyword: Anticoagulation system, PCI, Phase 3

Outcome measures

Primary outcome

Primary Endpoint: The primary efficacy endpoint is the composite of death,

nonfatal myocardial infarction, nonfatal stroke and urgent TLR through Day 3.

Secondary outcome

Secondary Endpoints:

1. The composite of death, nonfatal myocardial infarction, nonfatal stroke,

urgent TLR and stent thrombosis (including intra-procedural) through Day 3;

2. Major non-CABG bleeding (BARC Types 3 and 5) through Day 3;

3. The composite of death, nonfatal myocardial infarction, nonfatal stroke and

urgent TLR through Day 30;

4. The composite of death, nonfatal myocardial infarction, nonfatal stroke and

urgent TLR in Subgroup A (cardiac biomarker-positive patients) through Day 3;

5. The composite of death, nonfatal myocardial infarction, nonfatal stroke and

urgent TLR in Subgroups B and C (cardiac biomarker-negative patients) through

Day 3;

6. Major non-CABG bleeding (BARC Types 3 and 5) through Day 30.

Study description

Background summary

The study is being designed to determine if the REG1 Anticoagulation System is better compared to bivalirudin (marketed as Angiox) therapy for patients undergoing a procedure called PCI (percutaneous coronary intervention). A PCI is a procedure in which a blockage in an artery is opened using either a balloon (angioplasty), a metal mesh to hold open your blocked artery (stent), or a procedure to remove a clot (thrombectomy) or a combination of any of these procedures. The difference will be measured in terms of death, nonfatal heart attack, nonfatal stroke, certain complications that sometimes occur during and/or after the procedure, or return of a blockage that is being opened.

Study objective

Primary
To determine the efficacy of REG1 compared to bivalirudin in patients 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.

Secondary
The secondary objectives of this study are to:
1. Determine the efficacy of REG1 compared to bivalirudin for preventing the composite of death, nonfatal myocardial infarction, nonfatal stroke, urgent TLR and stent thrombosis (including intra-procedural) through Day 3.
2. Determine the safety of REG1 compared to bivalirudin on major hemorrhagic complications of PCI through Day 3 and Day 30.
3. Determine the efficacy of REG1 compared to bivalirudin for preventing the composite of death, nonfatal myocardial infarction, nonfatal stroke and urgent TLR through Day 30.
4. Determine the efficacy of REG1 compared to bivalirudin in cardiac biomarker-positive patients for preventing the composite of death, nonfatal myocardial infarction, nonfatal stroke and urgent TLR through Day 3.
5. Determine the efficacy of REG1 compared to bivalirudin in cardiac biomarker-negative patients for preventing the composite of death, nonfatal myocardial infarction, nonfatal stroke and urgent TLR through Day 3.

Study design

After signing the Informed Consent Form a screening procedure will start.

During or after a heart catheterization the decision to proceed to PCI will be made by your Study Doctor. After it is determined that the patient will require PCI he/she will be assigned by chance (like the flip of a coin) to either the REG1 study drug group, or to the bivalirudin group. Bivalirudin is an available marketed blood thinner drug that is commonly used in the catheterization lab during PCI procedures. The chance of receiving REG1 versus bivalirudin is a 1 in 2 chance. The patient and Study Doctor will know which anticoagulant the patient is going to receive (pegnivacogin or bivalirudin). Pegnivacogin, anivamersen and bivalirudin are given through an intravenous catheter (I.V.).

The participation in the study will last between 30 days and 6 months and will include about 3-4 visits, including your hospitalization, one outpatient visit (if the patient leaves the hospital on the same day as the PCI procedure) and 1-2 follow-up phone calls. The study team will follow the patient's progress closely and contact the patient about 3 days after PCI to see how they are doing during the participation. Blood samples will be drawn for the study and information about the patient, the PCI procedure and recovery information will be collected. The total amount of blood taken for this study is about 80 ml. After the 6 month status check, the participation in the study will be complete and no additional follow-up with the study team will be required.

Intervention

The REG1 Anticoagulation System (REG1) is a system consisting of a drug component (pegnivacogin) and the active control agent specific to pegnivacogin (anivamersen) VS Bivalirudin.The test products (pegnivacogin and anivamersen) and control (bivalirudin) will be administered in an open label fashion.

Study burden and risks

The risks and burden to the patient are thought to be in perspective to the treatment of the patient and the need to study new comounds with added benefits.

Monitoring of AE's, ECG's, vital signs and lab safety tests will be performed to support patient safety and evaluation of the safety profile.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. The study population will consist of patients with CAD undergoing PCI. Three key subgroups will be included as follows:
a. Subgroup A: Patients with ischemic symptoms at rest and positive cardiac biomarkers (troponin I or T or creatine kinase-MB) related to an acute coronary syndrome event within 7 days;
b. Subgroup B: Patients not meeting criteria for Subgroup A with at least one of the following risk factors:
* Current presentation with an acute coronary syndrome
with positive cardiac biomarkers > 7 days prior to randomization
* Current presentation with unstable angina (ACS without positive
cardiac biomarkers)
* Age >70 years
* Diabetes
* Chronic kidney disease (estimated CrCl < 60 mL/min)
* Planned multivessel PCI
* Prior CABG surgery
* Peripheral vascular disease;
c. Subgroup C: Patients with negative cardiac biomarkers and no risk factor, thereby not meeting criteria for Subgroup A or B;
2. Willing and able to sign an Institutional Review Board/Ethics Committee (IRB/EC) approved

informed consent prior to any study-related activities;
3. Male or female age 18 or greater;
4. If female of childbearing potential, must have a negative urine or serum pregnancy test or be post-menopausal for at least 1 year prior to randomization. Females of childbearing potential and males with partners of childbearing potential must
be using effective contraception to be eligible. Women who are nursing or lactating should not nurse while in the study as
the effects of this drug on nursing has not been studied. It is the Investigator*s responsibility for determining whether the patient is
using effective contraception and refraining from nursing for study participation;
5. Subject is able and willing to comply with the protocol and all study procedures,
including but not limited to the 20 + 4 hour blood draw, Endpoint (Day 3 +7), End-of-Study (Day 30), and 6-month vital status assessments.

Exclusion criteria

1. Acute ST-segment elevation myocardial infarction within 48 hours of randomization; of the following:
2. Evidence of current clinical instability including the following:
a. Sustained systolic blood pressure <90 mm Hg or cardiogenic shock;
b. Suspected acute myocarditis, pericarditis, endocarditis, or cardiac tamponade;
c. Suspected dissecting aortic aneurysm;
3. Evidence of a contraindication to anticoagulation or increased risk of bleeding such as:
a. Any evidence or history of intracranial bleeding or intracranial aneurysm;
b. Known hypercoagulable state, including treatment for malignancy (excluding basal cell skin carcinoma) in the past year, or coagulopathy with abnormal bleeding tendency;
c. History of intraocular hemorrhage other than due to diabetic retinopathy;
d. History of thrombocytopenia associated with abnormal bleeding;
e. History of thrombocytosis associated with a thrombotic event;
f. Severe trauma, fracture, major surgery, or biopsy of a parenchymal organ within 3 months;
g. Prolonged cardiopulmonary resuscitation within 3 months;
h. Major gastrointestinal bleeding within 3 months;
i. Spontaneous genitourinary bleeding within 3 months;
j. Any planned additional invasive procedure within 30 days after randomization;
4. Use of any investigational drug or device within 30 days of randomization or the planned use of an investigational drug or device through EOS (Day 30 follow-up);
5. Use of the following antithrombotic agents:
a. Fibrinolytic agents within 48 hours;
b. GP IIb/IIIa inhibitors within 24 hours;
c. Bivalirudin within 24 hours
d. Prior exposure to any component of REG1;
6. Baseline hemoglobin (Hgb) <9 g/dL or equivalent;
7. Renal impairment as determined by any one of the following:

a. Baseline estimated glomerular filtration rate (GFR) * 10 mL/min/1.73m²;
b. Currently undergoing renal replacement therapy (hemodialysis or peritoneal dialysis);
c. Degree of renal impairment for which use of bivalirudin is prohibited or contraindicated per local label instructions;
8. Baseline platelet count <100,000/mm3
9. Known allergy or intolerance to aspirin, to all available ADP/P2Y12 inhibitors (clopidogrel, prasugrel, ticagrelor), or to bivalirudin or REG1 (or any of their respective components);
;
10. The following planned procedures:
a. Planned staged PCI procedure within 30 days after randomization;
b. Planned CABG or valve surgery within 30 days after randomization;
11. Any other medical or psychiatric condition that in the Investigator*s judgment precludes participation in the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2014
Enrollment:	405
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	bivalirudin

Generic name:	Angiox
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	REG1 Anticoagulation System
Generic name:	anivamersen; pegnivacogin

Ethics review

Approved WMO Date:	10-10-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	07-11-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-04-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-05-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-05-2014
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-001384-23-NL
CCMO	NL46316.056.13