# A Randomized, Double-blind, Double-dummy, Active-controlled, Parallel-group, Multicenter Study to Compare the Safety of Rivaroxaban versus Acetylsalicylic Acid in Addition to Either Clopidogrel or Ticagrelor Therapy in Subjects with Acute Coronary Syndrome

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To estimate the bleeding risk with rivaroxaban, compared with ASA, in addition to a singleantiplatelet agent (clopidogrel or ticagrelor), in subjects with a recent ACS .

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Myocardial disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON42240

**Source**
ToetsingOnline

**Brief title**
GEMINI ACS 1

### Condition

- Myocardial disorders

**Synonym**
Infarction, unstable angina

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Janssen-Cilag
**Source(s) of monetary or material Support:** Janssen B.V.

## Intervention

**Keyword:** Acute Coronary Syndrome, Anticoagulans, Myocardial Infarction, Unstable Angina

## Outcome measures

### Primary outcome

The primary endpoint of the study is the composite of TIMI clinically

significant bleeding events that

consists of non CABG-related TIMI major bleeding events, TIMI minor bleeding

events, and TIMI

bleeding events requiring medical attention.

### Secondary outcome

The efficacy of Rivaroxaban compared with ASA, in addition to a single

antipletelet agent (clopidogrel or ticagrelor), will be explored, in reducing

the risk of the composite of CV death, MI, ischemic stroke and stent thrombosis

in subjects with a recent ACS.

# Study description

### Background summary

Rivaroxaban (JNJ-39039039; BAY 59-7939) is an oral anticoagulant. The mechanism of action of
rivaroxaban is to selectively and directly inhibit Factor Xa (FXa), which plays a central role in the

cascade of blood coagulation by mediating thrombin formation. Rivaroxaban does not require metabolic
conversion or a cofactor to exert its activity.
Rivaroxaban is marketed under the trade name XARELTO® and has been approved worldwide for the
treatment of multiple thrombosis-mediated conditions. XARELTO co-administered with acetylsalicylic
acid (ASA) alone or with ASA plus clopidogrel or ticlopidine has been approved in the European Union
(EU) for the prevention of atherothrombotic events in adult patients after an acute coronary syndrome
(ACS) with elevated cardiac biomarkers.

**Study objective**

To estimate the bleeding risk with rivaroxaban, compared with ASA, in addition to a single
antiplatelet agent (clopidogrel or ticagrelor), in subjects with a recent ACS .

**Study design**

This is a prospective, randomized, double-blind, double-dummy, active-controlled, parallel-group,
multicenter study to evaluate the safety and efficacy of rivaroxaban 2.5 mg twice daily compared with
ASA 100 mg once daily, in addition to a single antiplatelet agent (clopidogrel 75 mg once daily or
ticagrelor 90 mg twice daily), for a minimum of 180 days, and up to 360 days of treatment, in subjects
with a recent ACS (STEMI or NSTE-ACS). The number of subjects with STEMI enrolled in the study
will be limited to no more than 50% of all subjects.
Approximately 3,000 eligible subjects receiving maintenance treatment of ASA plus clopidogrel or ASA
plus ticagrelor for ACS will be stratified by the background P2Y12 inhibitor used. All subjects must
receive dual antiplatelet therapy (DAPT; ASA in combination with a P2Y12 inhibitor, clopidogrel or
ticagrelor) for treatment of the index event for a minimum of 48 hours prior to randomization. When
treatment with P2Y12 inhibitor has changed during the screening period, the stratification will be based on
the P2Y12 inhibitor used for the immediate 48 hours prior to randomization, and with the intention to
continue after randomization. Approximately 1,500 subjects are planned for enrollment in each stratum.

The selection of the P2Y12 inhibitor, clopidogrel or ticagrelor, will be made at least 48 hours prior to
randomization by the managing physician, and maintained throughout the study, except in cases where
discontinuation is medically indicated. It is strongly recommended that the intended duration of P2Y12
treatment should be consistent with societal guidelines for patients with ACS (eg, the American Heart
Association/American College of Cardiology Foundation guidelines, the European Society of Cardiology
guidelines), which recommend that P2Y12 treatment be maintained up to or over 12 months.

**Intervention**

PAtient will be assigned rivaroxaban + placebo together with ticagrelor or clopidogrel ór ASA + placebo togehter with ticagrelor or clopidogrel.
There are 2 treatment groups in this study:
• Rivaroxaban 2,5mg b.i.d.
• Aspirin 100mg

**Study burden and risks**

For side effects related to Rivaroxaban, ASA, Clopidogrel and Prasugrel I refer to the Informed Consent Form (appendix C).
Side effects from tests:
• Blood draw: Taking blood may cause bruising at the place where the needle goes into the skin. Fainting, and in rare cases infection, may occur.

# Contacts

**Public**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- Participants, 18 years or older, must have symptoms suggestive of acute coronary syndrome (ACS) (angina, or symptoms thought to be equivalent) within 48 hours of hospital presentation, or developed ACS while being hospitalized, and has a diagnosis of:
a) ST segment elevation myocardial infarction (STEMI);
b) non-ST-segment elevation acute coronary syndrome (NSTE-ACS).
However, participant who is 54 years of age or younger must also have either diabetes mellitus or a history of a prior myocardial infarction (MI), in addition to the presenting ACS event ;- Participant must be randomized within the screening window of 10 days after hospital admission for the index ACS event. Participant should have received acute phase treatment for the index ACS, such as intravenous anticoagulant or antiplatelet, and are receiving maintenance dual antiplatelet therapy (DAPT) with either clopidogrel plus acetyl salicylic acid (ASA), or ticagrelor plus ASA, with the intent to continue the treatment with a platelet adenosine diphosphate P2Y12 receptor antagonist (P2Y12 inhibitor) after randomization;;- Participants must agree to provide a pharmacogenomics deoxyribonucleic acid (DNA) sample

## Exclusion criteria

- Participant has any conditions that, in the opinion of the investigator, contraindicates anticoagulant therapy or would have an unacceptable risk;- Participant with a prior stroke of any etiology or transient ischemic attack (TIA);- Participant who received thrombolytic therapy as treatment for the index ACS event cannot be enrolled in the ticagrelor stratum ;- Participant has anticipated need for chronic administration of omeprazole or esomeprazole concomitantly with clopidogrel ;- Participant has known allergy or intolerance to ASA or rivaroxaban

# Study design

## Design

| | |
|---|---|
| Study phase: | 2 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Active |
| Primary purpose: | Treatment |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 13-03-2015 |
| Enrollment: | 130 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | Asaflow |
| Generic name: | Acetylsalicylzuut |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Brilique |
| Generic name: | Ticagrelor |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Plavix |
| Generic name: | Clopidogrel |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Xarelto |

| | |
|---|---|
| Generic name: | Rivaroxaban |
| Registration: | Yes - NL outside intended use |

## Ethics review

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| Approved WMO Date: | 02-02-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 20-03-2015 |
| Application type: | First submission |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-04-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 13-05-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 10-06-2015 |
| Application type: | Amendment |
| Review commission: | BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen) |
| Approved WMO Date: | 06-07-2015 |
| 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 | EUCTR2014-004266-26-NL |
| ClinicalTrials.gov | NCT02293395 |
| CCMO | NL52090.056.15 |