A randomized controlled trial of rivaroxaban for the prevention of major cardiovascular events in patients with coronary or peripheral artery disease (COMPASS - Cardiovascular OutcoMes for People using Anticoagulation StrategieS)

Published: 07-05-2013
Last updated: 24-04-2024

Primary objectives:*To determine whether rivaroxaban 2.5 mg twice daily (bid) + aspirin 100 mg once daily (od) compared with aspirin 100 mg od reduces therisk of a composite of myocardial infarction, stroke, or cardiovascular death in subjects with...

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

Summary

ID

NL-OMON47095

Source
ToetsingOnline

Brief title
COMPASS

Condition

- Coronary artery disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
coronary and peripheral artery disease; atherosclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Bayer B.V.
Source(s) of monetary or material Support: Bayer AG

Intervention

Keyword: CAD, COMPASS, PAD, rivaroxaban

Outcome measures

Primary outcome

Efficacy: Composite of myocardial infarction, stroke, or cardiovascular death.

Safety: modified International Society on Thrombosis and Haemostasis major

bleeding.

LTOLE: the same primary safety and efficacy variables will be collected.

Secondary outcome

Composite of myocardial infarction, stroke, cardiovascular death,

revasculatization and venous thromboembolism and cardiovascular hospitalization.

Mortality.

Upper gastrointestinal bleeding, ulceration, and gastrointestinal obstruction

or perforation.

Study description

Background summary

COMPASS is a Phase III trial that will investigate the prevention of major adverse cardiac events (MACE) including cardiovascular death, myocardial infarction and stroke in patients with coronary artery disease (CAD) or peripheral artery disease (PAD).
The COMPASS study will assess the potential of rivaroxaban to provide additional prevention of cardiovascular events to patients when added to aspirin, as well as investigating rivaroxaban and aspirin as single treatments. Patients will also be randomized to receive a proton pump inhibitor.

Study objective

Primary objectives:
*To determine whether rivaroxaban 2.5 mg twice daily (bid) + aspirin 100 mg once daily (od) compared with aspirin 100 mg od reduces the risk of a composite of myocardial infarction, stroke, or cardiovascular death in subjects with CAD or PAD
*To determine whether rivaroxaban 5 mg bid compared with aspirin 100 mg od reduces the risk of a composite of myocardial infarction, stroke or cardiovascular death in subjects with CAD or PAD

Secondary objectives:
*To determine whether each of rivaroxaban 2.5 mg bid + aspirin 100 mg od and rivaroxaban 5 mg bid alone reduces the risk of the composite of major thrombotic events (coronary heart disease, myocardial infarction, ischemic stroke, acute limb ischemia; cardiovascular death) compared with aspirin 100 mg od in subjects with CAD or PAD
*To determine whether each of rivaroxaban 2.5 mg bid + aspirin 100 mg od and rivaroxaban 5 mg bid alone reduces the risk of mortality in subjects with CAD or PAD

Objective for Long-Term Open-Label Extension (LTOLE)
To make rivaroxaban 2.5 mg twice daily (bid) + aspirin 100 mg once daily (od) available to COMPASS trial subjects until the rivaroxaban treatment is commercially available for this indication or for approximately 3 years from regulatory approval of LTOLE in a country, whichever comes first.

Study design

Randomized, double-blind, controlled phase III trial with a 3 x 2 partial factorial design.
Screening, run-in, follow-up and washout periods.
The run-in period will occur during the 30 days prior to initiation of study treatment, with the exception of subjects randomized after CABG who will not require a run-in. These patients will not be enrolled in NL. During run-in, subjects will discontinue any current anticoagulant therapy and will begin rivaroxaban placebo and 100 mg aspirin.

Treatment will begin on Day 0, which will also signal the initiation of the follow-up period. Subjects will be randomized 1:1 to pantoprazole or pantoprazole placebo and then will be randomized 1:1:1 to rivaroxaban and aspirin or their matching placebos:
- Rivaroxaban 2.5 mg bid + Aspirin 100 mg od + Pantoprazole 40 mg od
- Rivaroxaban 2.5 mg bid + Aspirin 100 mg od + Pantoprazole placebo
- Rivaroxaban 5 mg bid + Aspirin placebo + Pantoprazole 40 mg od
- Rivaroxaban 5 mg bid + Aspirin placebo + Pantoprazole placebo
- Rivaroxaban placebo + Aspirin 100 mg od + Pantoprazole 40 mg od
- Rivaroxaban placebo + Aspirin 100 mg od + Pantoprazole placebo
NB: Subjects already taking a proton pump inhibitor at baseline will undergo only a single randomization (to rivaroxaban 2.5 mg bid + aspirin 100 mg od, rivaroxaban 5 mg bid + aspirin placebo or rivaroxaban placebo + aspirin 100 mg od).

NL will not participate in both substudies (proteomics and brain MRI).

A final follow-up visit will occur when a minimum of 2,200 subjects experience an event for the primary efficacy outcome.
Patient numbers wordwide: enrolled = 29.940; randomized = 27.400.
Independent data safety monitoring board.

LTOLE: open label uncontrolled study

Intervention

Treatment with
rivaroxaban or placebo,
aspirine or placebo,
pantoprazole or placebo.

LTOLE: bi daily 2.5mg rivaroxaban and once daily 100mg aspirine

Study burden and risks

Risk: Adverse events of the study medication, in particular increased bleeding (if any).
Burden: The study is designed to closely follow routine clinical practice, therefore the burden to patients from the study related procedures including the blood sampling and visits is expected to be minimal. Approx. 17 study visits when study duration = 5 years.

LTOLE:
Risk: Adverse events of the study medication, in particular increased bleeding (if any).
Burden: The study is designed to closely follow routine clinical practice,

therefore the burden to patients from the study related procedures including the potential blood sampling and visits is expected to be minimal. Approx. 7 study visits when study duration = 3 years.

Contacts

Public
Bayer B.V.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

CAD or PAD (see protocol for definitions) plus at least one of the following:
o Age *65
o Age <65 plus documented atherosclerosis in two vascular beds or at least 2 additional risk factors (see protocol for details) ;All subjects randomized to the COMPASS trial willing to consent to LTOLE are
eligible unless the subjects developed a condition considered by the investigator as exclusionary.

* Subjects who have given their written informed consent to participate in the LTOLE after having received adequate information prior to any LTOLE specific procedures.

Exclusion criteria

- High risk of bleeding
- Stroke within 1 month or any history of hemorrhagic or lacunar stroke
- Ejection fraction <30% or NYHA class III or IV symptoms
- eGFR<15 mL/min
- Need for dual antiplatelet therapy, other non-aspirin antiplatelet therapy or oral anticoagulant therapy
- Systemic treatment with strong CYP 3A4 and P-gp inhibitors
- Inadequate contraception for females of childbearing potential
- Pregnancy, breast feeding;Subjects should not be included in the LTOLE study if, in the judgement of the investigator, they have
developed a condition which should exclude them from receiving LTOLE study medication. For example if the subject has developed atrial fibrillation or had a severe allergic rash while in the study, which subsided when drug was stopped and returned when drug was reinitiated.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-07-2013
Enrollment:	1350

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Aspirin
Generic name:	aspirin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Pantozol
Generic name:	pantoprazole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Xarelto
Generic name:	rivaroxaban
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-05-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-05-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-05-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-06-2013

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-07-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-08-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-08-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-08-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-09-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-01-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	11-02-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-02-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-03-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-04-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-08-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	21-05-2015
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-06-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-11-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-01-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-04-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-11-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-01-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	07-06-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-06-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-12-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-09-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	clinicaltrials.gov; registratienummer n.n.b.
EudraCT	EUCTR2012-004180-43-NL
CCMO	NL43921.060.13