Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivAroxaban-based antithrombotic strategy to an antipLatelet-based strategy after transcatheter aortIc vaLve rEplacement (TAVR) to Optimize clinical outcomes.

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To assess whether a rivaroxaban-based anticoagulation strategy, following successful TAVR, compared to an antiplatelet-based strategy, is superior in reducing death or first thromboembolic events (DTE).To assess the primary bleeding events (PBE) of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Interventional

Summary

ID

NL-OMON45994

Source
ToetsingOnline

Brief title
GALILEO

Condition

- Cardiac valve disorders

Synonym
Heart Valve replacement, Transcatheter Aortic Valve Replacement (TAVR)

Research involving
Human

Sponsors and support

Primary sponsor: Bayer
Source(s) of monetary or material Support: Opdrachtgever/Sponsor Bayer

Intervention

Keyword: Antiplatelet based strategy, Rivaroxaban based antithrombotic strategy, TAVR

Outcome measures

Primary outcome

Primary Efficacy Endpoint: death or first adjudicated thromboembolic event

(DTE) defined as the composite of allcause death and adjudicated any stroke,

myocardial infarction (MI), symptomatic valve thrombosis, pulmonary embolism

(PE), deep vein thrombosis (DVT), or non-CNS systemic embolism.

Primary Safety Endpoint: primary bleeding event (PBE) defined as the composite

of adjudicated life-threatening, disabling or major bleeding, classified

according to the valve academic research consortium (VARC) definitions

following the bleeding academic research consortium (BARC) classification.

Secondary outcome

The composite of TIMI major or minor bleeds

ISTH major bleeding

The composite of BARC 2, 3, or 5 bleeding

Study description

Background summary

Calcific aortic valve stenosis is characterized by an increased thrombogenic and inflammatory profile (2). Long-term oral antithrombotic treatment after TAVR aims to prevent complications, notably ischemic stroke and MI as well as thrombo-embolism related to deep vein thrombosis, pulmonary embolism, valve thrombosis, or systemic embolism while minimizing bleeding risk. The baseline risk for ischemic and thromboembolic complications is determined by comorbidities such as concomitant coronary artery disease (CAD), which is present in 20-70% of patients eligible for TAVR. Furthermore, in-hospital AF may occur in about one-third of patients referred for TAVR (20). Therefore, the actual standard of care after TAVR, i.e. DAPT, is not optimal in targeting the underlying pathophysiological mechanisms in severe AS. Rivaroxaban, through the inhibition
of the pathways underlying the increased thrombogenicity, may effectively prevent Integrated Clinical Study Protocol No. 17938 28 SEP 2015 Version: 2.0 Page: 22 of 94 thrombotic complications after TAVR without exposing this elderly (57) population to an increased bleeding risk.

Study objective

To assess whether a rivaroxaban-based anticoagulation strategy, following successful TAVR, compared to an antiplatelet-based strategy, is superior in reducing death or first thromboembolic events (DTE).

To assess the primary bleeding events (PBE) of the rivaroxaban-based strategy, followingTAVR, compared to an antiplatelet-based strategy.

Study design

Event-driven, randomized, open-label with blinded endpoint evaluation, parallel-group, active-controlled, multicenter international study.

Intervention

Rivaroxaban-based strategy:
The first dose of rivaroxaban (10 mg once-daily) is given either immediately after randomization or within 24-72 hours after the last intake of clopidogrel. Rivaroxaban 10 mg once-daily can be taken with or without food. ASA 75-100 mg once-daily is to be continued unchanged or started immediately after randomization if not already being taken. ASA is discontinued after 90 days from randomization. Rivaroxaban is continued until the efficacy cut-off date,

i.e. when the predefined number of efficacy endpoints is reached. In the event of NOAF the dose of rivaroxaban is switched from 10 mg once-daily to 20 or 15 mg once-daily, depending on renal function. Rivaroxaban 20 and 15 mg once-daily should be taken with food. Up to 90 days after randomization, ASA 75-100 mg once-daily is to be continued unchanged. After 90 days from randomization, ASA is discontinued and rivaroxaban 20 or 15 mg once-daily is continued alone until the efficacy cut-off date.

Antiplatelet-based strategy:
Clopidogrel 75 mg once-daily and ASA 75-100 mg once-daily are to be continued unchanged, or to be started at the time of randomization if not already being taken. In subjects that are clopidogrel-naïve at randomization a single loading dose of at least 300 mg clopidogrel should be administered followed by clopidogrel 75 mg once-daily. Clopidogrel must be discontinued at 90 days post-randomization and ASA 75-100 mg once-daily is to be continued until the efficacy cut-off date.In the event of NOAF, the antiplatelet-based strategy will be stopped and a VKA with a target INR 2-3 started. ASA 75-100mg once-daily is to be continued in combination with VKA until 90 days after randomization. After 90 days, ASA must be discontinued and VKA continued alone until the efficacy cut-off date.

Study burden and risks

Medication risks:
thrombocythemia
liver disease
dizziness headache
muscle Haemorrhage
bleeding
medication allergy and shortness of breath

Contacts

Public
Bayer

N/A N/A
Leverkusen 51368
DE
Scientific
Bayer

N/A N/A
Leverkusen 51368

DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Key inclusion criteria:
• Successful TAVR of a native aortic valve stenosis (either native of valve-in-valve)
• By iliofemoral or subclavian access
• With any approved/marketed device
• Written informed consent (IC)

Exclusion criteria

Key exclusion criteria:
• Atrial fibrillation (AF), current or previous, with an ongoing indication for oral anticoagulant treatment
• Any other indication for continued treatment with any oral anticoagulant (OAC)
• Known bleeding diathesis (such as but not limited to active internal bleeding, clinically significant bleeding, platelet count <= 50,000/mm3 at screening, hemoglobin level < 8.5 g/dL, active peptic ulcer or known gastrointestinal (GI) bleeding, history of intracranial hemorrhage or subdural hematoma)
• Any ongoing absolute indication for dual-antiplatelet therapy (DAPT) at time of screening that is unrelated to the TAVR procedure.
• Clinically overt stroke within the last 3 months
• Planned coronary or vascular intervention or major surgery
• Severe renal impairment (eGFR < 30 mL/min/1.73 m2) or on dialysis, or post-TAVR unresolved acute kidney injury with renal dysfunction stage 2 or higher
• Moderate and severe hepatic impairement (Child-Pugh Class B or C) or any hepatic disease associated with coagulopathy.

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:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-12-2015
Enrollment:	120
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Acenocoumarol
Generic name:	Sintrom
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	aspro clear
Generic name:	ascetylsalicylacid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Phenprocoumon
Generic name:	Marcoumar
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	plavix

Generic name:	clopidogrel
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Rivaroxaban
Generic name:	Xarelto
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-12-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-12-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2015-001975-30-NL
ClinicalTrials.gov	NCT02556203
CCMO	NL55198.018.15