A prospective Randomised, open label, blinded endpoint (PROBE) study to Evaluate DUAL antithrombotic therapy with dabigatran etexilate (110mg and 150mg b.i.d.) plus clopidogrel or ticagrelor vs. triple therapy strategy with warfarin (INR 2.0 - 3.0) plus clopidogrel or ticagrelor and aspirin in patients with non valvular atrial fibrillation (NVAF) that have undergone a percutaneous coronary intervention (PCI) with stenting

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See section 2.2 of the protocol.The main objective of this study is to compare a DAT regimen of 110mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (110mg DE-DAT) and 150mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (...

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

Summary

ID

NL-OMON44285

Source
ToetsingOnline

Brief title
RE-DUAL PCI

Condition

- Cardiac arrhythmias
- Embolism and thrombosis

Synonym
non-valvular atrial fibrillation and percutaneous coronary intervention

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Boehringer Ingelheim bv

Intervention

Keyword: dabigatran etexilate, NVAF, PCI

Outcome measures

Primary outcome

See section 5.1.1 of the protocol.

The primary endpoint for this trial is a safety endpoint; time to first ISTH

Major or Clinically Relevant Non-Major Bleeding Event

Secondary outcome

See section 5.1.2 of the protocol.

The secondary endpoints of efficacy are (all time to first event):

1. A combined endpoint of thrombotic events or death (DTE: all death + MI +

stroke/SE) and unplanned revascularisation by PCI/CABG

2. A combined endpoint of thrombotic events or death (DTE: all death + MI +

stroke/SE)

3. Individual outcome events:

**All death (Cardiovascular, Non-cardiovascular, Undetermined)

**MI

**Stroke

**SE

**Stent thrombosis

4. Composite endpoint of death + MI + stroke

5. Repeated revascularisation by PCI/CABG

Study description

Background summary

See section 1.1 of the protocol.

The current estimate of the prevalence of atrial fibrillation (AF) in the developed world is approximately 1.5*2% of the general population. The arrhythmia is associated with a fivefold increase in the risk of stroke and a three-fold increase in the incidence of congestive heart failure and higher mortality. Twenty to thirty percent of non valvular AF (NVAF) patients have concomitant coronary artery disease.

In patients undergoing PCI, the addition of clopidogrel to aspirin (ASA) reduces death, myocardial infarction (MI) and stroke. When patients with AF that are receiving anticoagulant treatment have to undergo a PCI with stenting, there is an indication for concomitant treatment with ASA and clopidogrel (triple antithrombotic therapy (TAT)) to prevent stent thrombosis.

Rigorous antithrombotic treatment invariably raises the risk of bleeding, adding to a poorer prognosis with an estimated five-fold mortality increase following MI. An acceptable bleeding risk while maintaining a lower ischaemic event rate is considered a must in the post-PCI setting.

In patients with ACS or undergoing PCI, the presence of AF raises a therapeutic challenge because treatment with both anticoagulant and antiplatelet therapies

is preferred to prevent stroke and further coronary events.

Studies suggest there might be a potential benefit with the implementation of a dual antithrombotic therapy (DAT) regimen (anticoagulant plus clopidogrel) in comparison with a TAT regimen (anticoagulant plus clopidogrel plus ASA) in NVAF that have undergone PCI.

Study objective

See section 2.2 of the protocol.

The main objective of this study is to compare a DAT regimen of 110mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (110mg DE-DAT) and 150mg dabigatran etexilate b.i.d. plus clopidogrel or ticagrelor (150mg DE-DAT) with a TAT combination of warfarin plus clopidogrel or ticagrelor plus ASA * 100mg once daily (q.d.) (warfarin-TAT) in patients with NVAF that undergo a PCI with stenting (elective or due to an ACS).

Study design

See section 3.1 of the protocol.

This is a prospective, randomised, open label, blinded endpoint (PROBE), active comparator trial and the clinical endpoints are being adjudicated by an IAC in a blinded fashion. Patients will be consented and screened after undergoing a successful PCI.

Patients aged < 80 years will be randomly assigned to 110mg dabigatran etexilate b.i.d., 150mg dabigatran etexilate b.i.d. or warfarin in a 1:1:1 ratio for the duration of the trial.
Patients aged *80 years will be randomly assigned depending on their geographical location:
**Patients aged *80 years in the USA will be assigned to 110mg dabigatran etexilate b.i.d., 150mg dabigatran etexilate b.i.d. or warfarin in a 1:1:1 ratio
**All other patients aged *80 years outside of the USA will be assigned to 110mg dabigatran etexilate or warfarin in a 1:1 ratio.

In addition to their randomised treatment:
**All patients will receive either clopidogrel (75mg q.d.) or ticagrelor (90mg b.i.d), according to the local label, for at least 12 months after randomisation.
**Patients randomised to receive warfarin will receive ASA (* 100mg q.d.) for either one month in patients with a bare metal stent BMS and for three months in patients with a DES.

Intervention

Treatment with dabigatran etexilate instead of VKA.

Study burden and risks

Considering a study duration of 31 months, the following study activities will be done:

- Physical exam * 2x
- Blood pressure * 9x
- ECG * 5x
- Blood draw * 10x
- INR monitoring (warfarin group) * every 2-4 weeks, 4ml per blood sample
- Urine pregnancy test * 10x

Contacts

Public
Boehringer Ingelheim

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NL
Scientific
Boehringer Ingelheim

Comeniusstraat 6
Alkmaar 1817 MS
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Male or female patients aged ><=18 years;- Patients with Non Valvular Atrial Fibrillation;- Patient presenting with:;An ACS (STEMI, NonSTEMI [NSTEMI] or unstable angina [UA]) that was successfully treated by PCI and stenting (either Bare Metal Stent or Drug Eluting Stent);Or;Stable Coronary Artery Disease with at least one lesion eligible for PCI that was successfully treated by elective PCI and stenting (either BMS or DES) ;- The patient must be able to give informed consent in accordance with International Conference on Harmonisation Good Clinical Practice guidelines and local legislation and/or regulations.

Exclusion criteria

- Patients with a mechanical or biological heart valve prosthesis;- Cardiogenic shock during current hospitalisation;- Stroke within 1 month prior to screening visit;- Patients who have had major surgery within the month prior to screening;- Gastrointestinal haemorrhage within one month prior to screening, unless, in the opinion of the Investigator, the cause has been permanently eliminated;- Major bleeding episode including life-threatening bleeding episode in one month prior to screening visit;- Anaemia (haemoglobin <=10g/dL) or thrombocytopenia including heparin-induced thrombocytopenia (platelet count <=100 x 109/L) at screening;- Severe renal impairment (estimated CrCl calculated by Cockcroft-Gault equation) <=30mL/min at screening;- Active liver disease

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):	05-02-2015
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Coumadin
Generic name:	warfarin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Pradaxa
Generic name:	dabigatran etexilate

Ethics review

Approved WMO Date:	16-07-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-09-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-11-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-12-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	31-12-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-01-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-02-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-07-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-10-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United

	(Nieuwegein)
Approved WMO Date:	11-11-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-01-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-03-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-04-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-05-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-06-2016
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-01-2017

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
EudraCT	EUCTR2013-003201-26-NL
CCMO	NL49746.060.14