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Anticoagulation using the direct factor Xa inhibitor apixaban during Atrial Fibrillation catheter Ablation: Comparison to vitamin K antagonist therapy

Submission date
16/06/2014

Recruitment status
No longer recruiting

Registration date
20/06/2014

Overall study status
Completed

Last Edited
13/05/2019

Condition category
Circulatory System

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Atrial fibrillation (AF) is a common heart condition which causes an irregular and rapid heartbeat. People with AF can be of much greater risk of having a stroke than the general population, depending on the presence of additional risk factors (high blood pressure, for example). Reducing this risk has traditionally been via the use of vitamin K antagonists, anticoagulation drugs that reduce blood clotting and thrombosis (blood clots within a blood vessel). Factor Xa inhibitors and direct thrombin inhibitors are new, novel fixed dose oral anticoagulants (NOACS). These NOACS - apixaban, rivaroxaban and dabigatron have all been shown to prevent stroke in patients with AF and have now been approved for use in the USA, Canada and Europe. The use of NOACS are also recommended in the current guidelines for AF treatment. Between 5-15% of AF patients undergo a procedure to treat their condition called catheter ablation, where radiofrequency energy is used to destroy the area inside the heart that is causing the abnormal beating. While some of these patients are on long-term anticoagulation therapy due to their risk of stroke, all patients undergoing this procedure have to take them in a period just before and after the operation to reduce the risk of a stroke associated with the actual procedure. Some small observational studies have highlighted concerns with using NOACS in patients undergoing catheter ablation. One study investigating the use of dabigatran showed that 4.4% of patients treated with this drug during catheter ablation suffered severe complications such as fluid developing around the heart (pericardial tamponade), stroke and, in some cases, the patients died. This was compared with only 2.1% of patients suffering similar events when VKAs was used. Although it is likely that the results of this study occurred by chance (as since demonstrated by other observational studies), it does mean that the present data suggests that VKAs should be the treatment of choice during catheter ablation. The international consensus statement on AF catheter ablation was published before these reports on dabigatran. It suggests to perform AF catheter ablation on continuous anticoagulation using either a VKA or a NOAC. The focussed update of the European Society of Cardiology (ESC) guidelines on AF,

however, published after these reports on dabigatran became available, only mentions using a VKA. The aim of this study is to test whether NOACs can be safely and effectively used for catheter ablation of AF.

Who can participate?
Patients who have AF, are going to undergo catheter ablation and are at an increased risk of stroke (have, for example, had a previous stroke, are aged at least 75 years, have high blood pressure, diabetes mellitus or symptomatic heart failure)

What does the study involve?
Comparison of two therapies: NOACs and VKAs during the atrial fibrillation ablation procedure

What are the possible benefits and risks of participating?
The patient will receive a particularly thorough medical examination as part of the participation in the study. Beyond that, no further personal health benefits, besides the usual standard of care, are expected for the patient. In the AXAFA study, no investigational drugs or interventions not yet approved by health authorities will be applied. All study drugs are market approved and will be used within the approved indications, for AF only. All concomitant study procedures and therapies, e. g. the catheter ablation for AF, are standard care procedures according to applicable medical guidelines.

Where is the study run from?
8 EU countries: Austria, Germany, Italy, Spain, Belgium, Netherlands, UK, Denmark, USA

When is the study starting and how long is it expected to run for?
January 2015 – September 2017

Who is funding the study?
Kompetenznetz Vorhofflimmern e.V. (AFNET)
[Atrial Fibrillation NETwork] (Germany)

Who is the main contact?
Elisabeth Freund
e.freund@cri-muc.eu

Contact information

Type(s)
Scientific

Contact name
Prof Paulus Kirchhof

Contact details
c/o Elisabeth Freund
Head of Clinical Operations
CRI - The Clinical Research Institute GmbH
Arnulfstraße 19
München
Germany
80335

Additional identifiers

EudraCT/CTIS number
2014-002442-45

IRAS number

ClinicalTrials.gov number
NCT02227550

Secondary identifying numbers
N/A

Study information

Scientific Title
Anticoagulation using the direct factor Xa inhibitor apixaban during atrial fibrillation catheter ablation and comparison to vitamin K antagonist therapy: A investigator-initiated, prospective, parallel-group, randomised, open, blinded outcome assessment (PROBE) interventional multi-centre trial.

Acronym
AXAFA-AFNET5

Study objectives
Anticoagulation with the direct factor Xa inhibitor apixaban is not less safe than VKA therapy in patients undergoing catheter ablation of non-valvular AF in the prevention of peri-procedural complications.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee at the Medical Faculty of the University of Leipzig (Ethik-Kommission an der Medizinischen Fakultät der Universität Leipzig), 20/01/2015, ref: 341/14-ff

Study design
Prospective phase IV parallel-group randomised open, blinded outcome assessment (PROBE) interventional multi-centre trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Non-valvular atrial fibrillation with a clinical indication for catheter ablation/bleeding + stroke risk/cardiology

Interventions
Anticoagulation therapy with new oral anticoagulants and vitamin-k-antagonists during atrial fibrillation ablation

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Test IMP: Apixaban, comparator IMP: locally used VKA

Primary outcome measure
A composite of
1. All-cause death
2. Stroke (ischemic stroke, subarachnoid hemorrhage and hemorrhagic stroke)
3. Major bleeding events, defined as BARC 2 or higher

Secondary outcome measures
1. Any bleeding event
2. Major bleeding events according to the ISTH and TIMI definitions
3. Number of strokes, other systemic embolic events, and all-cause deaths
4. Time from randomisation to ablation
5. Nights spent in hospital after ablation
6. Health-care related cost calculation
7. Number of hospitalizations for cardiovascular reasons
8. Treatment duration prior to ablation and total time on oral anticoagulation
9. Number of patients with clinically indicated TEE
10. ACT during ablation
11. Time to recurrent AF
12. Rhythm status at the end of follow-up
13. Vascular access complications leading to prolongation of in-hospital stay or specific therapy
14. Quality-of-life changes at month 3 compared to baseline
15. Cognitive function change at month 3 compared to baseline
Updated 18/10/2017:
16. MRI sub-study, only: Prevalence of clinically “silent” MRI-detected brain lesions within 48 hours after the ablation procedure
17. MRI sub-study, only: Impact of ablation-associated clinically overt strokes or MRI-detected but clinically “silent” acute brain lesions on cognitive function after ablation

Overall study start date
01/01/2015

Completion date
12/09/2017

Eligibility

Key inclusion criteria
1. Non-valvular AF (ECG-documented) with a clinical indication for catheter ablation
2. Clinical indication to undergo catheter ablation on continuous anticoagulant therapy
3. Presence of at least one of the CHADS2 stroke risk factors
3a. Stroke or TIA
3b. Age ≥75 years
3c. Hypertension, defined as chronic treatment for hypertension, estimated need for continuous antihypertensive therapy or resting blood pressure >145/90 mm Hg
3d. Diabetes mellitus
3e. Symptomatic heart failure (NYHA ≥II)
4. Age ≥18 years
5. Provision of signed informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
630

Total final enrolment
674

Key exclusion criteria
General exclusion criteria
1. Any disease that limits life expectancy to less than 1 year
2. Participation in another clinical trial, either within the past two months or still ongoing
3. Previous participation in AXAFA
4. Pregnant women or women of childbearing potential not on adequate birth control: only women with a highly effective method of contraception (oral contraception or intra-uterine device) or sterile women can be randomised.
5. Breastfeeding women
6. Drug abuse or clinically manifest alcohol abuse
Added 18/10/2017:

7. Any stroke within 14 days before randomisation
8. Coadministration with drugs that are strong dual inhibitors of cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) or strong dual inducers of CYP3A4 and P-gp (Appendix VIII)

Exclusion criteria related to a cardiac condition
9. Valvular AF (as defined by the focussed update of the ESC guidelines on AF, i.e. severe mitral valve stenosis, mechanical heart valve). Furthermore, patients who underwent mitral valve repair are not eligible for AXAFA.
10. Any previous ablation or surgical therapy for AF
11. Cardiac ablation therapy for any indication (catheter-based or surgical) within 3 months prior to randomisation
12. Clinical need for triple therapy (combination therapy of clopidogrel, acetylsalicylic acid, and oral anticoagulation)
13. Other contraindications for use of VKA or apixaban

Exclusion criteria based on laboratory abnormalities
14. Severe chronic kidney disease with an estimated glomerular filtration rate (GFR) <15 ml/min
Added 18/10/2017: 15. Documented atrial thrombi less than 3 months prior to randomisation

Date of first enrolment
01/01/2015

Date of final enrolment
10/04/2017

Locations

Countries of recruitment
Austria

Belgium

Denmark

Germany

Italy

Netherlands

Spain

United Kingdom

United States of America

Study participating centre

c/o Elisabeth Freund
München
Germany
80335

Sponsor information

Organisation
Kompetenznetz Vorhofflimmern e.V. (AFNET) [Atrial Fibrillation NETwork]

Sponsor details
Mendelstr. 11
Münster
Germany
48149

Sponsor type
Research organisation

Website
http://www.kompetenznetz-vorhofflimmern.de

ROR
https://ror.org/01spm3d88

Funder(s)

Funder type
Research organisation

Funder Name
Kompetenznetz Vorhofflimmern e.V. (AFNET) [Atrial Fibrillation NETwork]

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal.

Intention to publish date
18/03/2018

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	01/01/2017		Yes	No
Results article	results	21/08/2018	13/05/2019	Yes	No