Apixaban versus antiplatelet drugs or no antithrombotic drugs after anticoagulation-associated intracerebral haemorrhage in patients with atrial fibrillation. A randomised phase II clinical trial.

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Treatment with apixaban may be the best long-term alternative for the prevention of recurrent stroke and systemic thrombo-embolism in patients with atrial fibrillation who survived an anticoagulation-associated intracerebral haemorrhage,

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27026

Bron
Nationaal Trial Register

Verkorte titel
APACHE-AF

Aandoening

Apixban
Intracerebral haemorrhage
Antiplatelet drugs
Atrial fibrillation
Hersenbloeding
Plaatjesremmers
Atriumfibrilleren

Ondersteuning

Primaire sponsor: UMC Utrecht
Overige ondersteuning: Dutch Heart Foundation – Clinical Established Investigator grant to C.J.M. Klijn
ZonMw – Aspasia grant to C.J.M. Klijn

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The combination of vascular death or non-fatal stroke (cerebral infarction, intracerebral haemorrhage, or subarachnoid haemorrhage) during follow-up.

Toelichting onderzoek

Achtergrond van het onderzoek

There is a marked lack of evidence on the optimal prevention of ischaemic stroke in patients with atrial fibrillation and a recent intracerebral haemorrhage (ICH) during treatment with oral anticoagulation. These patients are currently treated with vitamin K antagonists, antiplatelet drugs, or no antithrombotic treatment, depending on personal and institutional preferences. Treatment with a direct oral anticoagulant like apixaban might be an attractive alternative in terms of a low risk of recurrent ICH, while at the same time being effective for the prevention of ischaemic stroke.
This study aims to obtain reliable estimates of the rates of vascular death or non-fatal stroke in patients with atrial fibrillation and a recent anticoagulation-associated intracerebral haemorrhage who are treated with apixaban versus those who are treated with antiplatelet drugs or no antithrombotic drug at all.

This study has a multi-centre, phase II, randomised, open-label clinical trial with blinded outcome assessment design.

Doel van het onderzoek

Treatment with apixaban may be the best long-term alternative for the prevention of recurrent stroke and systemic thrombo-embolism in patients with atrial fibrillation who survived an anticoagulation-associated intracerebral haemorrhage,

Onderzoeksopzet

All endpoints: for the duration of the study.
Functional outcome at 6 and 12 months.

Onderzoeksproduct en/of interventie

Patients will be randomised between:

-apixaban 5 mg orally twice daily

-treatment with one or two oral APDs (acetylsalicylic acid, carbasalate calcium, clopidogrel, or dipyridamole) or no antithrombotic treatment at all, at the discretion of the treating physician.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

- Intracerebral haemorrhage, documented with CT or MRI, during treatment with anticoagulation (VKA, any direct thrombin inhibitor, any factor Xa inhibitor, or (low-molecular-weight) heparin at a therapeutic dose).

- The haemorrhage has occurred between 7 and 90 days before randomization.

- Diagnosis of (paroxysmal) non-valvular AF, documented on electrocardiography.

- A CHA2DS2VASc score ≥ 3.

- Score on the modified Rankin scale (mRS) ≤4.

- Equipoise regarding the optimal medical treatment for the prevention of stroke. The clinical equipoise should be self-reported by the attending neurologist after reviewing all relevant information available for the individual patient.

- Age ≥ 18 years.

- Written informed consent by the patient or by a legal representative

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

- Conditions other than atrial fibrillation for which the patient requires long-term anticoagulation.

- A different clinical indication for the use of an APD, such as clopidogrel for recent coronary stenting.

- Rheumatic mitral valve disease, a prosthetic heart valve, or mitral valve repair.

- Serious bleeding event in the previous 6 months, except for intracerebral haemorrhage.

- High risk of bleeding (e.g., active peptic ulcer disease, a platelet count of <100,000.mL-1 or haemoglobin level of <6.206 mMol.L-1, ischemic stroke in the previous 7 days (patients are eligible thereafter), documented haemorrhagic tendencies, or blood dyscrasias).

- Current alcohol or drug abuse.

- Life expectancy of less than 1 year.

- Severe renal insufficiency (a serum creatinine level of more than 221 µmol per liter or a calculated creatinine clearance of <25 ml per minute).

- Alanine aminotransferase or aspartate aminotransferase level greater than 2 times the upper limit of the normal range or a total bilirubin more than 1.5 times the upper limit of the normal range, unless an benign causative factor, other than moderate or severe liver disease, (e.g. Gilbert’s syndrome) is known or identified.

- Allergy to apixaban.

- Use of strong cytochrome P450 3A4 (CYP3A4) and P-glycoprotein (P-gp) inhibitors (e.g. systemic azole-antimycotics as ketoconazole or HIV protease inhibitors such as ritonavir).

- Pregnancy or breastfeeding.

- Women of childbearing potential: any woman who has begun menstruation and is not menopausal or otherwise permanently unable to conceive. A post-menopausal woman is defined as a woman who is over the age of 45 and has not had a menstrual period for at least 12 months.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Actieve controle groep

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	23-09-2014
Aantal proefpersonen:	100
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	16-04-2014
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 50507
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4395
NTR-old	NTR4526
CCMO	NL47761.041.14
OMON	NL-OMON50507

Resultaten