

# Early treatment of atrial fibrillation for stroke prevention trial

<b>Submission date</b> 07/12/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 10/01/2011	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 20/05/2025	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Current plain English summary as of 19/08/2020:

### Background and study aims

Atrial fibrillation is a heart condition that results in an irregular, often abnormally fast heart rate, which also increases the risk of having a stroke. It can be treated with anti-arrhythmic drugs that restore a normal heart rhythm and rate. It can also be treated with catheter ablation, a procedure where the diseased area of the heart is very carefully destroyed to interrupt the fast, irregular electrical impulses. The aim of this study is to find out whether early, structured rhythm control treatment using anti-arrhythmic drugs and catheter ablation can prevent complications (e.g., stroke) in patients with atrial fibrillation.

### Who can participate?

Patients aged 18 and over who have had atrial fibrillation for a year or less and are at high risk of stroke

### What does the study involve?

Patients are randomly allocated to receive early treatment or usual care. In the early treatment group, patients receive either catheter ablation or anti-arrhythmic drug treatment at an early timepoint. The initial treatment is selected by the doctor. If atrial fibrillation returns both treatments are combined. Usual care follows the current guidelines for atrial fibrillation treatment. All patients are followed up every 6 months by questionnaire and by outpatient follow-up visits at 12, 24 and 36 months.

### What are the possible benefits and risks of participating?

Not provided at time of registration

### Where is the study run from?

CRI - The Clinical Research Institute GmbH (Germany)

### When is the study starting and how long is it expected to run for?

July 2011 to May 2020 (updated 19/08/2020, previously: December 2019)

Who is funding the study?

German Atrial Fibrillation Network (Germany)

Sanofi (Germany)

Abbot (Germany)

Deutsche Herzstiftung e.V. (Germany)

European Heart rhythm Association (EHRA)

BMBF (German Ministry for Science)

Deutsches Zentrum für Herz-Kreislauf-forschung (DZHK) (Germany)

Who is the main contact?

Prof Paulus Kirchhof

Previous plain English summary:

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Prof Paulus Kirchhof, east@cri-muc.eu

**Study website**

<http://www.easttrial.org> and <https://www.kompetenznetz-vorhofflimmern.de/en/patientinformation/studies/east-afnet-4>

# Contact information

## Type(s)

Scientific

## Contact name

Prof Paulus Kirchhof

## Contact details

University Heart and Vascular Center UKE, Department of Cardiology  
Martinistraße 52, Gebäude Ost 70  
Hamburg  
Germany  
20246

# Additional identifiers

## EudraCT/CTIS number

2010-021258-20

## IRAS number

## ClinicalTrials.gov number

NCT01288352

## Secondary identifying numbers

Nil known

# Study information

## Scientific Title

An investigator-driven, prospective, parallel-group, randomised, open, blinded outcome assessment (PROBE-design), multicentre trial for the prevention of stroke in high-risk subjects with atrial fibrillation

## Acronym

EAST-AFNET 4

## Study objectives

EAST prospectively tests the hypothesis that an early, structured rhythm control therapy based on anti-arrhythmic drugs and catheter ablation can prevent atrial fibrillation (AF) related complications in patients with AF when compared to usual care.

Patients will be randomised to early therapy or usual care. In the early therapy group, patients will receive either catheter ablation (usually by pulmonary vein isolation), or adequate anti-arrhythmic drug therapy at an early timepoint. The initial therapy will be selected by the local investigator. Upon AF recurrence, both modalities will be combined. Usual care will be conducted following the current ESC guidelines for AF treatment. Early rhythm control therapy will be guided by ECG monitoring.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Ethikkommission der Ärztekammer Westfalen-Lippe und der Medizinischen Fakultät der Westfälischen Wilhelms-Universität Münster, 09/02/2011, ref: 2010-274-f-A

**Study design**

Phase IV randomized open prospective two-armed parallel-group multicentre trial

**Primary study design**

Interventional

**Secondary study design**

Randomised parallel trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

**Participant information sheet**

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

**Health condition(s) or problem(s) studied**

Recent onset atrial fibrillation/stroke risk

**Interventions**

Usual care group:

Usual care closely follows the suggestions laid out in the current ESC guidelines for AF. In addition to anti-thrombotic therapy and therapy of underlying heart disease, usual care usually consists of an initial attempt to control symptoms by rate control therapy (Metoprolol, Bisoprolol, Digoxin, Digitoxin, Verapamil). Rhythm control interventions are only indicated when symptoms cannot be controlled by optimal rate control therapy in the usual care group.

Early therapy group:

Patients in the early therapy group will be treated following the same therapeutic recommendations of the ESC guidelines as the usual care group. In addition, rhythm control therapy will be initiated early with the aim of preventing recurrence and delaying or preventing progression of AF.

Early-onset rhythm control therapy can consist of:

1. Optimal antiarrhythmic drug therapy (Dronedarone, Amiodarone, Flecainide, Propafenone),
2. Catheter ablation with the aim of pulmonary vein isolation (PVI),
3. Anti-arrhythmic drug therapy and catheter ablation may be supplemented by early cardioversion in patients with persistent AF.

All individual treatment decisions will be taken by the treating study physician considering the labelling of the procedures and drugs and patient preferences.

**Duration:**

EAST is an event-driven trial, i.e. the trial will be terminated after 685 evaluable primary outcomes have occurred. A duration of the entire trial of around 8 years is expected. All patients will be followed-up until the end of the trial with a minimum follow-up period of two and a half years.

**Intervention Type**

Drug

**Phase**

Phase IV

**Drug/device/biological/vaccine name(s)**

Not provided at time of registration

**Primary outcome measure**

1. A composite of cardiovascular death, stroke/transient ischaemic attack (TIA), and hospitalisation due to worsening of heart failure or due to acute coronary syndrome
2. Nights spent in hospital per year

**Secondary outcome measures**

1. Cardiovascular death
2. Stroke/transient ischaemic attack
3. Worsening of heart failure assessed by hospitalisations
4. Acute coronary syndrome assessed by hospitalisations
5. Time to recurrent atrial fibrillation
6. Cardiovascular hospitalisations
7. All-cause hospitalisations
8. Left ventricular function assessed by transthoracic echocardiography at month 24 (+/- 2 months) after randomisation
9. Quality of life changes assessed by EQ-5D and 12-item short form health survey (SF-12) at month 24 (+/- 2 months) after randomisation
10. Cognitive function assessed by MoCA at month 24 (+/- 2 months) after randomisation

**Overall study start date**

01/07/2011

**Completion date**

29/05/2020

## **Eligibility**

**Key inclusion criteria**

1. Recent-onset AF (less than or equal to 1 year prior to enrolment)
2. At least one ECG within recent 12 months that documents AF whereas the AF episode must last longer than 30 seconds
3. One of the following:

- 3.1. Aged greater than 75 years, or
- 3.2. Prior stroke or transient ischaemic attack
- OR two of the following:
- 3.3. Aged greater than 65 years
- 3.3. Female sex
- 3.4. Arterial hypertension (chronic treatment for hypertension, estimated need for continuous antihypertensive therapy or resting blood pressure greater than 145/90 mmHg)
- 3.5. Diabetes mellitus
- 3.6. Severe coronary artery disease (previous myocardial infarction, coronary artery bypass graft [CABG] or percutaneous coronary intervention [PCI])
- 3.7. Stable heart failure (New York Heart Association [NYHA] II or left ventricular ejection fraction [LVEF] less than 50%)
- 3.8. Left ventricular hypertrophy on echocardiography (more than 15 mm wall thickness)
- 3.9. Chronic kidney disease (Modified Diet in Renal Disease [MDRD] stage III or IV)
- 3.10. Peripheral artery disease
- 4. Provision of signed informed consent
- 5. Age greater than or equal to 18 years

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

2745 (first patient in on 28/07/2011)

**Total final enrolment**

2789

**Key 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 ongoing
- 3. Previous participation in the EAST trial
- 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 (IUD)] or sterile women can be randomised
- 5. Breastfeeding women
- 6. Drug abuse
- 7. Prior AF ablation or surgical therapy of AF
- 8. Previous therapy failure on amiodarone, e.g. patients who suffered from symptomatic recurrent AF that required escalation of therapy while on amiodarone
- 9. Patients not suitable for rhythm control of AF
- 10. Severe mitral valve stenosis
- 11. Prosthetic mitral valve

- 12. Clinically relevant hepatic dysfunction requiring specific therapy
- 13. Clinically manifest thyroid dysfunction requiring therapy. After successful treatment of thyroid dysfunction, patients may be enrolled when their thyroid function is controlled.
- 14. Severe renal dysfunction (stage V, requiring or almost requiring dialysis)

**Date of first enrolment**

01/07/2011

**Date of final enrolment**

31/12/2016

## **Locations**

**Countries of recruitment**

Belgium

Czech Republic

Denmark

France

Germany

Italy

Netherlands

Poland

Spain

Switzerland

United Kingdom

**Study participating centre**

**CRI - The Clinical Research Institute GmbH**

München

Germany

80335

## **Sponsor information**

**Organisation**

German Atrial Fibrillation Network (Germany)

**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**

German Atrial Fibrillation Network

**Funder Name**

Sanofi

**Alternative Name(s)**

sanofi-aventis, Sanofi US, Sanofi-Aventis U.S. LLC, Sanofi U.S.

**Funding Body Type**

Government organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

**Funder Name**

Abbott Pharmaceuticals

**Alternative Name(s)**



**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United States of America

**Funder Name**

Deutsche Herzstiftung e.V.

**Funder Name**

European Heart rhythm Association (EHRA)

**Funder Name**

BMBF (German Ministry for Science)

**Funder Name**

Deutsches Zentrum für Herz-Kreislauf-forschung (DZHK)

## Results and Publications

**Publication and dissemination plan**

Not provided at time of registration

**Intention to publish date****Individual participant data (IPD) sharing plan**

Not provided at time of registration

**IPD sharing plan summary**

Not provided at time of registration

**Study outputs**

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	01/11/2011		Yes	No
<a href="#">Other publications</a>	rationale and design	01/09/2013		Yes	No

<a href="#">Other publications</a>	article	01/02/2015		Yes	No
<a href="#">Results article</a>	results	01/10/2020	02/09/2020	Yes	No
<a href="#">Results article</a>	Subanalysis of patients with heart failure	30/07/2021	02/08/2021	Yes	No
<a href="#">Results article</a>	Subanalysis in asymptomatic patients	27/08/2021	31/08/2021	Yes	No
<a href="#">Results article</a>	Analysis of treatment patterns	02/09/2021	03/09/2021	Yes	No
<a href="#">Results article</a>	Association between pattern of atrial fibrillation and outcomes	26/07/2022	22/07/2022	Yes	No
<a href="#">Results article</a>		15/08/2022	16/08/2022	Yes	No
<a href="#">Results article</a>	Early rhythm control	29/08/2022	30/08/2022	Yes	No
<a href="#">Results article</a>	subgroup analysis for early rhythm-control therapy	01/01/2023	16/12/2022	Yes	No
<a href="#">Results article</a>	Association of genetic risk and outcomes in patients with atrial fibrillation: interactions with early rhythm control in the EAST-AFNET4 trial	02/06/2023	02/06/2023	Yes	No
<a href="#">Results article</a>	Safety and efficacy of long-term sodium channel blocker therapy for early rhythm control	04/05/2024	07/05/2024	Yes	No
<a href="#">Results article</a>	Safety and efficacy of amiodarone and dronedarone for early rhythm control in EAST-AFNET 4	19/05/2025	20/05/2025	Yes	No