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Early treatment of atrial fibrillation for stroke prevention trial

Submission date	Recruitment status	[X] Prospectively registered
07/12/2010	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
10/01/2011	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/11/2025	Circulatory System	

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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Who is the main contact?
Prof Paulus Kirchhof, east@cri-muc.eu

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

Clinical Trials Information System (CTIS)
2010-021258-20

ClinicalTrials.gov (NCT)
NCT01288352

Protocol serial number
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

Study type(s)
Treatment

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 occured. 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(s)
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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

Belgium

Czech Republic

Denmark

France

Germany

Italy

Netherlands

Poland

Spain

Switzerland

Study participating centre
CRI - The Clinical Research Institute GmbH
München
Germany
80335

Sponsor information

Organisation
German Atrial Fibrillation Network (Germany)

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

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?
Results article	results	01/10/2020	02/09/2020	Yes	No
Results article	Subanalysis of patients with heart failure	30/07/2021	02/08/2021	Yes	No
Results article	Subanalysis in asymptomatic patients	27/08/2021	31/08/2021	Yes	No
Results article	Analysis of treatment patterns	02/09/2021	03/09/2021	Yes	No
Results article	Association between pattern of atrial fibrillation and outcomes	26/07/2022	22/07/2022	Yes	No
Results article		15/08/2022	16/08/2022	Yes	No
Results article	Early rhythm control	29/08/2022	30/08/2022	Yes	No
Results article	subgroup analysis for early rhythm-control therapy	01/01/2023	16/12/2022	Yes	No
Results article	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
Results article	Safety and efficacy of long-term sodium channel blocker therapy for early rhythm control	04/05/2024	07/05/2024	Yes	No
Results article	Safety and efficacy of amiodarone and dronedarone for early rhythm control in EAST-AFNET 4	19/05/2025	20/05/2025	Yes	No
Results article	Estimated atrial fibrillation burden on early rhythm-control and cardiovascular events	01/09/2025	04/11/2025	Yes	No
Protocol article	protocol	01/11/2011		Yes	No
Other publications	rationale and design	01/09/2013		Yes	No
Other publications	article	01/02/2015		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes