ATRIAL FIBRILLATION
NETWORK

EASThigh - AFNET 11

STUDIENDESIGN

Early Atrial Fibrillation Ablation For Stroke Prevention In Patients With high Comorbidity Burden.

The EAST^{high}-AFNET 11 trial

Global Cardiovascular Research Funders Forum

Else Kröner Fresenius Stiftung

GCP-Service International

Medtronic

Hartstichting

clinicaltrials.gov NCT06324188

Background of EAST^{high}-AFNET 11

- Despite improvements in the management of AF, patients remain at increased risk for cardiovascular complications.
- EAST-AFNET 4 demonstrated that systematic, early rhythm control reduced adverse cardiovascular outcomes by 21% compared to usual care.
- A subanalysis of EAST-AFNET 4 revealed a greater benefit of early rhythm control in patients with multiple comorbidities (CHA2DS2-VASc ≥4)
- 50-70% of all patients have a high comorbidity burden when their AF is first diagnosed.
- Attaining sinus rhythm is the key mediator for the outcome-reducing effect of early rhythm control.
- AF ablation is more effective than antiarrhythmic drugs for rhythm control and avoids long-term antiarrhythmic drug treatment, thus reducing polypharmacy.
- Nonetheless, AF ablation is rarely offered to patients with a high comorbidity burden, despite this group having potentially most to gain.

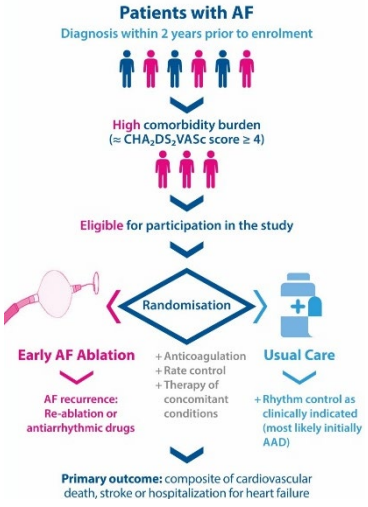
➢ Only an adequately powered randomized trial comparing early AF ablation to usual care, can resolve the role of early AF ablation in this population with a very high need for outcome reduction.

Study design of EAST^{high}-AFNET 11

Hypothesis:

Early AF ablation prevents cardiovascular complications in patients with AF and a high comorbidity burden (CHA_2DS_2VASc score ≥4) compared to usual care.

- Investigator-initiated, prospective, randomized, open, blinded endpoint assessment, multicenter trial, evaluating the effectiveness and safety of early AF ablation in patients with recently diagnosed AF and a high comorbidity burden compared to usual care.
- 2312 study participants will be included.
- Study participants will be randomized in a 1:1 ratio to one of two parallel therapy strategies: “Early AF Ablation” and “Usual Care”.
- All therapies are clinically approved and will be applied in their clinical indications following applicable medical guidelines (Treatment Strategy Trial) - study out of scope of MDR/MPDG --> §15 BO
- The standard ablation tool is the well-established Cryoballoon system from Medtronic.
- The study is event-driven with a fixed number of primary endpoint events (n=527) to be observed for testing superiority.



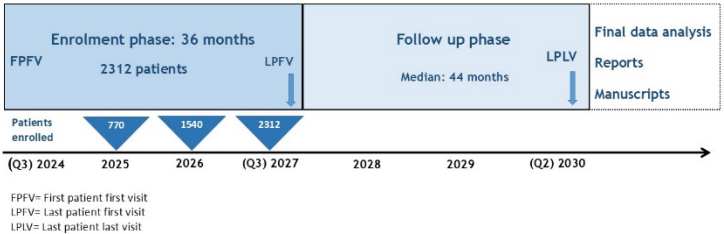
Study design of EAST^{high}-AFNET 11

- **Primary Outcome:** time from randomization to the 1st occurrence of either:
  - cardiovascular death,
  - stroke (either ischemic or hemorrhagic)
  - hospitalization for worsening of heart failure.

- **Primary safety outcome:** composite of all-cause death and serious complications of the AF therapy

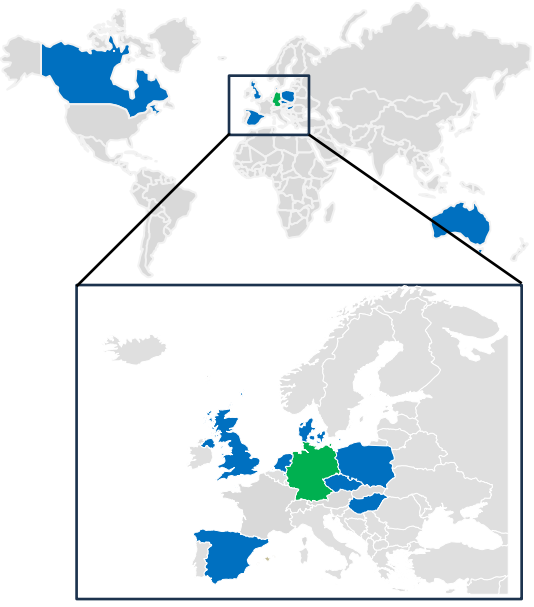
- **Secondary outcome parameters** address safety, health-economic outcomes, patient reported outcomes, and cognitive function.

- Study duration: about 6 years
- Recruitment phase: 36 months
- Follow up phase: median 44 months
- Patients will be followed up until end of study



Study design of EAST^{high}-AFNET 11

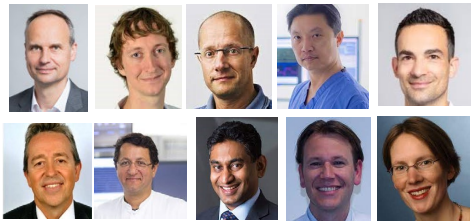
- The study will be conducted in about 10 countries, in about 200 study sites.
  Competitive enrolment
- Study sites will create local study clusters consisting of one ablation site **(A-site)** and additional non-ablating standard study sites **(S-sites)** (hospitals or office-based cardiologists).



Global	**N=2312**	**(100%)**
Australia:	n=195 patients	(8.4%)
Canada:	n=375 patients	(16.2%)
Germany:	n=610 patients	(26.3%)
The Netherlands:	n=225 patients	(9.7%)
UK:	n=325patients	(14.0 %)
Denmark:	n=145 patients	(6.3%)
Czech Republic:	n= 65 patients	(2.8%)
Hungary	n=100 patients	(4.3%)
Poland:	n=113 patients	(4.9%)
Spain:	n=165 patients	(7.1%)

Organisation of EAST^{high}-AFNET 11

- **Sponsor:** Atrial Fibrillation NETwork (AFNET), Münster
- **Academic SC members (GCRFF countries):** Paulus Kirchhof, Andreas Rillig, Jason Andrade, Jens Cosedis Nielsen, Andre Ng, Jose Merino, Prash Sanders, Kevin Vernooy, Antonia Zapf (statistician)
- EAST^{high}-AFNET 11 was endorsed by the Global Cardiovascular Research Funders Forum Dec 2022
- Investigator-initiated trial supported by public funders and Medtronic
- **Contract Research Organization (CRO):** GCP-Service International



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