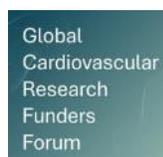




Early Atrial Fibrillation Ablation For Stroke Prevention In Patients With high Comorbidity Burden (EAST^{high}-AFNET 11)

ClinicalTrials.gov:
NCT06324188





EAST^{high}-AFNET 11: BACKGROUND



- 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.





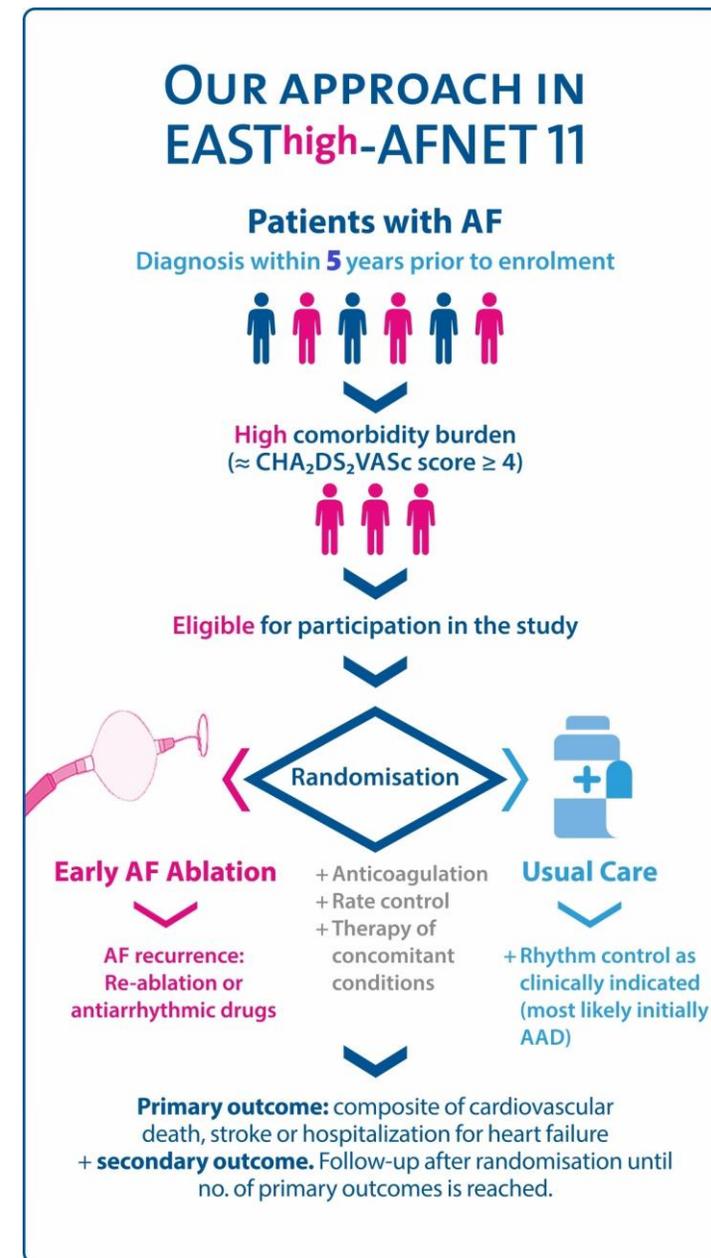
EAST^{high}-AFNET 11: HYPOTHESIS AND STUDY DESIGN

Hypothesis

- Early AF ablation prevents cardiovascular complications in patients with AF and a high comorbidity burden (CHA₂DS₂VASc score ≥4) compared to usual care.

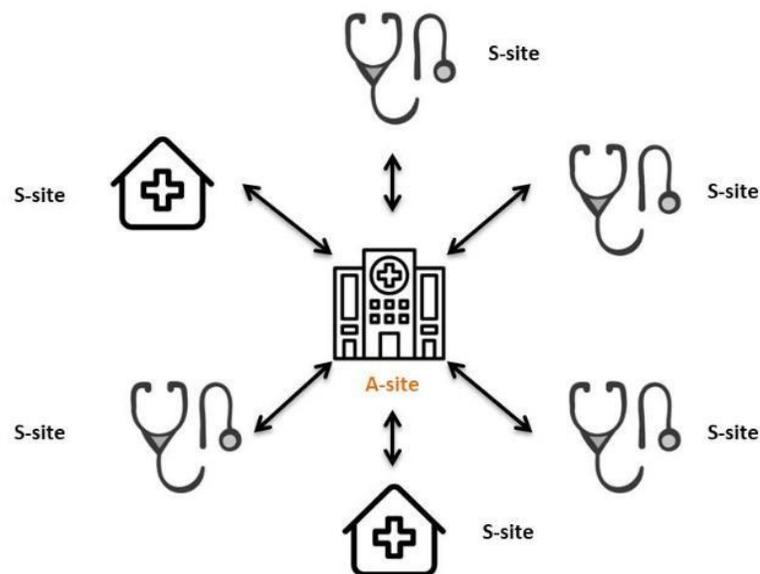
Study Design

- 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**)
- The study is event-driven with a fixed number of primary endpoint events (n=527) to be observed for testing superiority.





- **Primary Outcome:** time from randomization to the 1st occurrence of either:
 - cardiovascular death,
 - stroke (either ischemic or hemorrhagic)
 - hospitalization for worsening of heart failure.
- **An independent blinded Clinical Event Committee** will evaluate each SAE to determine if the reported SAE constitutes a **Clinical Event = Primary Endpoint** for the study.
- **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 sites cluster structure based on the successful experience of EAST-AFNET 4

- The study will be conducted in about **10 countries**, in about **200 study sites** → Competitive enrolment
- Participating ablation sites should have experience with AF ablation using the **cryoballoon or other ablation systems with comparable efficacy and safety from Medtronic**.
- 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).
- All study sites will screen, randomise, and follow study patients.
- S-site patients who are randomised to the “**Early AF Ablation**” group will be referred to the associated A-site for AF ablation only.
 - A-site performs ablation and completes Index ablation forms in eCRF
 - S-site manages the patient's further treatment and follow-up and completes remaining CRF forms



EAST^{high}-AFNET 11: ORGANISATION

- **Sponsor:** Atrial Fibrillation NETwork (AFNET)
- **Academic SC members:** Paulus Kirchhof, Andreas Rillig, Jason Andrade, Jens Cosedis Nielsen, Andre Ng, Jose Merino, Prash Sanders, Kevin Vernooy, Michał Orczykowski, Antonia Zapf (statistician), AFNET board members
- EAST^{high}-AFNET 11 is an international study and was endorsed by the GCRFF
- Investigator-initiated trial supported by public funders and Medtronic
- **Contract Research Organization:** GCP-Service International International

