Catalyst Trial: Clinical trial of atrial fibrillation patients comparing left atrial appendage occlusion therapy to non-vitamin K antagonist oral anticoagulants

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The objective of this trial is to evaluate the safety and effectiveness of the Amulet device compared to NOAC therapy in patients with non-valvular AF at increased risk for ischemic stroke and who are recommended for long-term NOAC therapy.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON54346

Source
ToetsingOnline

Brief title
Catalyst

Condition

- Cardiac arrhythmias

Synonym
atrial fibrillation, heart rhythm disorder

Research involving
Human

Sponsors and support

Primary sponsor: St. Jude Medical

Source(s) of monetary or material Support: Abbott

Intervention

Keyword: Amulet, Atrial Fibrillation, Left atrial appendage, NOAC, Strokeprevention

Outcome measures

Primary outcome

The clinical investigation has the following primary endpoints:

1. Composite of ischemic stroke, systemic embolism, or cardiovascular (CV)

mortality through 2 years (non-inferiority)

2. Major bleeding or CRNMB events, excluding procedure related events through 2

years (superiority)

3. Composite of ischemic stroke or systemic embolism through 3 years

(non-inferiority)

Secondary outcome

The following secondary endpoints will be tested when the primary endpoints are

met:

1. Major bleeding or CRNMB events through 2 years (non-inferiority)

2. Major bleeding or CRNMB events through 2 years (superiority)

3. Disabling or fatal strokes through 2 years (superiority)

Study description

Background summary

The rationale for conducting the clinical investigation is to evaluate the safety and effectiveness of the Amulet device compared to NOAC therapy in patients with non-valvular AF at increased risk for ischemic stroke and systemic embolism, and who are recommended for long-term NOAC therapy.

Investigations have shown LAAO and NOACs each perform favorably compared to warfarin for stroke risk reduction. However, data are lacking to evaluate LAAO vs NOACs for stroke prophylaxis. Therefore, this trial will randomize subjects between the Amulet LAA occlusion device (*Device Group*) and a commercially available NOAC medication (*Control Group*). Results of this trial could potentially offer a device-based approach for ischemic stroke prophylaxis as an alternative to long-term OAC.

Study objective

The objective of this trial is to evaluate the safety and effectiveness of the Amulet device compared to NOAC therapy in patients with non-valvular AF at increased risk for ischemic stroke and who are recommended for long-term NOAC therapy.

Study design

The clinical investigation is a prospective, randomized, multicenter active control worldwide trial. Subjects will be randomized in a 1:1 ratio between the Amulet LAA occlusion device (Device Group) anda commercially available NOAC medication (Control Group). The choice of NOAC in the Control Group will be left to study physician discretion.

Intervention

Approximately 2,650 subjects are randomized in a 1: 1 ratio.
In approximately 1325 subjects an Amulet device is placed to close the LAA and the other 1325 subjects receive the standard NOAC therapy.

Study burden and risks

Subjects in the control-group are not at extra risk because the treatment with NOAC therapy they receive during the study is the same as the standard treatment. The additional burden for these subjects is the burden in time. An additional MRI (or CT with radiation burden) may be required at the baseline visit if imaging of a previous stroke/TIA is not available.

Subjects in the Amulet group do not receive the standard treatment but the implantation of the Amulet device. The risks of the implantation are similar to other cardiac procedures. The radiation risk is equivalent to a diagnostic catheterization procedure. Risks associated to the Amulet implant are the same as any other device used to close an opening in the heart. These subjects will also undergo multiple transesophageal ultrasounds with the associated risks (see E9 of the ABR form). During the 12-month visit, the TEE can be replaced by a CT scan with the associated radiation risk, if occlusion of the atrial appendage is confirmed on a previous TEE.

6 weeks after implantation, the use of the anti-coagulant can be discontinued and the subject will continue to take daily aspirin up to and including the 12 month follow-up visit.

An additional MRI (or CT with radiation burden) may be required at the baseline visit if imaging of a previous stroke/TIA is not available.
If a neurological event occurs during the study and is confirmed via MRI/CT, a TEE or CT scan of the heart will be made within 7 days for the subjects in the Amulet group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Documented paroxysmal, persistent, or permanent non-valvular AF

(documentation must
include an electrocardiogram, Holter, or event recorder)
2. At high risk of stroke or systemic embolism, defined as a CHA2DS2-VASc score of >= 3 for women and >= for men
3. Eligible for long-term NOAC therapy
4. Able to comply with the required NOAC medication regimen if randomized to the Control Group
5. Able to comply with the required medication regimen post-device implant if subject is randomized
to the Device Group or subject is a Roll-in
6. Able to understand, and is willing to provide, written informed consent to participate in the trial,
prior to any clinical investigation related procedure or assessment
7. 18 years of age or older, or the age of legal consent
8. Able and willing to return for required follow-up visits and assessments

Exclusion criteria

1. Requires long-term OAC therapy for a condition other than AF
2. Planned cardiac intervention or surgery, which is invasive or requires sedation or anesthesia,
within 3 months following randomization, other than study-related procedures such as LAAO and
cardiac imaging (if applicable)
3. Known contraindication to, or allergic to, aspirin, clopidogrel, or OAC medication use
4. Indicated for P2Y12 platelet inhibitor for > 1 year post-randomization
5. In the opinion of the investigator, is considered at high risk for general anesthesia and general
anesthesia is planned for the study procedure
6. Has undergone atrial septal defect (ASD) repair or has an ASD closure device present
7. Has undergone patent foramen ovale (PFO) repair or has a PFO closure device implanted
8. Is implanted with a mechanical valve prosthesis
9. Is implanted with an inferior vena cava filter
10. History of rheumatic or congenital mitral valve heart disease
11. Has any of the customary contraindications for a percutaneous catheterization procedure
(e.g. subject is too small to accommodate the ICE probe (if planned) or required catheters,
or subject has active infection or bleeding disorder)
12. Customary contraindications for TEE/TOE (e.g., presence of esophageal varices, esophageal
stricture, or history of esophageal cancer)

13. Experienced stroke or transient ischemic attack (TIA) within 90 days prior to randomization or
implant procedure (as applicable)
14. Underwent any cardiac or non-cardiac intervention or surgery within 30 days prior to
randomization
15. Underwent catheter ablation for AF or atrial flutter within 60 days prior to randomization
16. Experienced myocardial infarction within 90 days prior to randomization
17. New York Heart Association Class IV Congestive Heart Failure
18. Left ventricular ejection fraction <= 30% (per most recent assessment)
19. Symptomatic carotid disease (defined as > 50% lumen diameter narrowing on CTA, MRA,
or TCD with symptoms of ipsilateral transient or visual TIA evidenced by amaurosis fugax,
ipsilateral hemispheric TIAs or ipsilateral stroke); if subject has a history of carotid stent or
endarterectomy the subject is eligible if there is < 50% lumen diameter narrowing
20. Has known intracranial atherosclerosis and/or intracranial small vessel disease (defined
as 6 points on the Fazekas Scale)
21. Reversible cause of AF (i.e., secondary to thyroid disorders, acute alcohol intoxication,
trauma, recent major surgical procedures)
22. History of idiopathic or recurrent venous thromboembolism
23. LAA is obliterated or surgically ligated
24. Thrombocytopenia (defined as < 50,000 platelets per microliter (<50 x 109 /L) or anemia
(defined as hemoglobin < 10 g/dL) requiring transfusions
25. Hypersensitivity to any portion of the device material or individual components of the
Amulet LAA occluder device (e.g., nickel allergy)
26. Actively enrolled in, or plans to enroll in, a concurrent clinical study in which the active
treatment arm may confound the results of this trial
27. Is pregnant or breastfeeding, or pregnancy is planned during the course of the
investigation
28. Active endocarditis or other infection producing bacteremia
29. Transient case of AF (i.e., never previously detected, provoked/induced by surgical or
catheter manipulations, etc.)
30. Severe renal failure (estimated glomerular filtration rate <30 ml/min/1.73m2), but not on
dialysis
31. Life expectancy is less than 2 years in the opinion of the Investigator

32. Presence of other anatomic or comorbid conditions, or other medical, social, or
psychological conditions that, in the Investigator*s opinion, could limit the subject*s ability
to participate in the clinical investigation or to comply with follow up requirements, or
impact the scientific soundness of the clinical investigation results.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-01-2023
Enrollment:	26
Type:	Actual

Medical products/devices used

Generic name:	Amplatzer AMULET LAA occluder
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	26-08-2021
Application type:	First submission

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-07-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	27-01-2023
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	11-07-2024
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04226547
CCMO	NL76115.100.21