VOLT-AF First-In-Human Study

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The VOLT AF First-in-Human (FIH) study will collect feasibility data to show that the Volt PFA System functions as intended in a clinical setting and to demonstrate acute safety and effectiveness for the treatment of symptomatic, recurrent...

Ethical review	Not approved
Status	Will not start
Health condition type	Cardiac arrhythmias
Study type	Interventional

Summary

ID

NL-OMON51674

Source
ToetsingOnline

Brief title
VOLT-AF

Condition

- Cardiac arrhythmias

Synonym
Atrium Fibrillation, heart rhythm disturbance

Research involving
Human

Sponsors and support

Primary sponsor: Abbott Medical
Source(s) of monetary or material Support: Abbott

Intervention

Keyword: Catheter, paroxysmal atrial fibrillation, persistent atrial fibrillation, Pulsed Field Ablation

Outcome measures

Primary outcome

Acute Safety:

Acute safety will be summarized as the rate of subjects experiencing a device and/or procedure-related serious adverse event with onset within 7-days of any ablation procedure (index or repeat procedure) that uses the Volt PFA System that are defined below:

- Atrio-esophageal fistula1
- Cardiac tamponade/perforation2
- Death
- Heart block
- Myocardial infarction
- Pericarditis3
- Phrenic nerve injury resulting in permanent diaphragmatic paralysis
- Pulmonary edema
- Pulmonary vein stenosis1
- Stroke/cerebrovascular accident
- Thromboembolism
- Transient ischemic attack
- Vagal nerve injury/gastroparesis
- Vascular access complications (including major bleeding events4)
- Device and/or procedure related cardiovascular and/or pulmonary adverse event

that prolongs hospitalization for more than 48 hours (excluding hospitalization solely for arrhythmia recurrence or non-urgent cardioversion)

Acute Effectiveness:

Acute procedural effectiveness will be summarized as the rate of pulmonary veins treated with the Volt PFA system that are isolated at the end of the index ablation procedure. Acute procedural failure for each pulmonary vein is defined as any of the following:

1. Inability to isolate a pulmonary vein at the end of the index ablation procedure. Isolation will be assessed via confirmation of electrical isolation in each ablated pulmonary vein after a minimum waiting period of 20 minutes via entrance block at a minimum. Touch-up ablation to achieve isolation will be allowed for any pulmonary vein reconnection detected during the index procedure with the investigational catheter (to the maximum delivery allowed per vein) and will not be considered a failure.
2. Any use of a non-study ablation device for pulmonary vein isolation.

Secondary outcome

1. 12-month effectiveness: Freedom from documented (symptomatic or asymptomatic) AF/AFL/AT episodes of >=30 seconds duration that are documented by protocol-specified 12-lead ECG, transtelephonic monitoring (TTM) or Holter monitor after the initial catheter ablation procedure through 12 months of follow-up (after a 90-day blanking period following the initial ablation procedure).

The situations in which subjects will be considered 12-month effectiveness endpoint failures are those listed below:

• Acute procedural failure occurs, defined as the inability to isolate all targeted pulmonary veins using only the Volt PFA Catheter for ablation. Isolation will be assessed via confirmation of electrical isolation (via entrance block at a minimum) in each ablated pulmonary vein after a minimum waiting period of 20 minutes.
• Any use of a non-study ablation device for pulmonary vein isolation or to deliver ablation lesions in the left atrium.
• If documented AF/AFL/AT recurrence (>30 second episode), excluding cavotricuspid-dependent atrial flutter that has been confirmed in an electrophysiology study (e.g. via entrainment maneuvers), occurs at any time after the blanking period (>90 days after the initial procedure) as assessed by protocol-specified 12-lead ECG, TTM, and Holter monitoring (NOTE: If the subject has a continuous atrial arrhythmia throughout a 12-lead ECG recording after the blanking period indicating AF/AFL/AT recurrence, this will be considered sufficient documentation of recurrence unless there is evidence that the recorded arrhythmia is short-lived and less than 30 seconds as determined by the investigator.).
• If subject requires a repeat procedure for the treatment of AF, non-CTI-dependent AFL, or AT using a non-study ablation device.
• Any use of a new class I or III AAD for AF after the blanking period.
• Any use of a class I or III AAD for AF at a dose higher than the historical

maximum dose for the subject.

• If the subject requires a cardioversion (electrical or pharmacological) for the treatment of AF/AFL/AT after the blanking period (excluding CTI-dependent AFL confirmed by entrainment maneuvers).

• Surgical treatment of AF/AFL/AT post index procedure.

AF/AFL/AT recurrence during the 90-day blanking period (<=90 days post-initial procedure) will not be considered a treatment failure. One repeat procedure for ablation of AF recurrence during the 90-day blanking period (performed 31-80 days post ablation) will not be considered a treatment failure so long as the investigational PFA catheter is used for PVI ablation. Use of a non-investigational catheter to achieve PVI or to deliver any additional ablation lesions in the left atrium during the first repeat procedure will be considered a treatment failure. A repeat procedure after the blanking period or a second repeat procedure at any time will be considered a treatment failure. After the 90-day blanking period, use of Class I or III antiarrhythmic drugs (AADs) will not count as a treatment failure provided that only previously failed AADs are taken at doses that do not exceed the previously failed dose.

AF/AFL/AT recurrence (for the purposes of assessing effectiveness endpoints) will only be assessed by protocol-specified 12-lead ECG, TTM, and Holter monitoring devices for assessment of this primary endpoint so that all subjects are monitored equally with devices of the same sensitivity and specificity. Collected ECG, TTM, and Holter data from sites will be evaluated by a physician

at a core laboratory for independent and unbiased assessment of AF/AFL/AT recurrence for endpoint analysis.

2. Additional acute effectiveness measures:

a. Rate of pulmonary veins treated with the Volt PFA system that are isolated at the end of the index ablation procedure when treated per protocol (to isolation or to maximum allowable treatment applications).

b. Rate of subjects with procedural success of PVI ablation with the Volt PFA System defined as in Section 4.1.2 in the PFA population and in the Per Protocol population (defined in Section 8.1), where inability to isolate any pulmonary vein would constitute a failure.

3. Proportion of subjects with successful first-pass isolation of all targeted veins, and proportion of all targeted pulmonary veins with successful first-pass PV isolation, where first pass isolation is defined as confirmation of entrance block in the ablated pulmonary vein following the initial minimum waiting period of 20 minutes without any ablation after the start of the 20-minute waiting period.

4. Proportion of subjects with reconnections, proportion of treated pulmonary veins ablated with reconnections, and locations of pulmonary vein reconnections (of treated veins) upon electro-anatomical remapping at 3 months.

5. Proportion of subjects that experience any procedure and/or Volt PFA System-related adverse event (AE) throughout the 12-month follow-up period.

6. 12-month single procedure effectiveness, defined as 12-month effectiveness as above after a single ablation procedure. Any repeat ablation procedure

required by the subject at any time will be deemed a failure.

7. Proportion of subjects requiring one or more repeat AF ablations at 12 months following the initial AF ablation procedure.

8. Changes in EQ-5D-5L and AFEQT scores from baseline to follow up at 3, 6, and 12-months after the initial procedure.

9. Procedure data, including but not limited to ablation data, mapping data, usage of Automark, usage of the LivePoint, method(s) used for catheter placement (e.g. fluoroscopy, intracardiac ultrasound, etc.), procedure time, fluoroscopy time, total ablation time, LA dwell time, time to perform PVI, and number and location of PFA energy applications.

10. Cardiovascular-related health care utilization through 12-months after the initial procedure, including but not limited to, cardiovascular or AF-related hospitalization (includes readmission) or emergency visit, cardioversion, repeat ablations, use of AADs after 3-month blanking period, and primary SAEs.

11. Arrhythmia monitoring (12-lead ECG, HM, and TTM) compliance

12. Change in PV diameter from baseline to 30 days and 3 months post procedure.

13. Incidence, number, size (diameter and volume) and anatomic location of cerebral lesions detected on post-procedure brain MRI compared to pre-procedure brain MRI.

Study description

Background summary

AF is associated with mortality and comorbidities such as stroke, heart failure, and sudden cardiac death. In a meta-analysis of contemporary,

well-controlled, randomized clinical trials in AF, the average annual stroke rate was 1.5%, and annualized death rate was 3% in anticoagulated AF patients.6 A minority of these deaths are related to stroke, while sudden cardiac death and death from progressive heart failure are more frequent, emphasizing the need for interventions beyond anticoagulation.7, 8 Atrial fibrillation is also associated with high rates of hospitalization. This hospitalization is commonly for AF management, but is also often due to heart failure, myocardial infarction, and treatment associated complications. 9, 10 Additionally, patients with AF have significantly poorer quality of life than healthy controls, experiencing a variety of symptoms including lethargy, palpitations, dyspnea, chest pain, sleeping difficulties, and mental distress.10-14

The current conventional approach to perform catheter ablation is via thermal energy such as cryoablation or radiofrequency (RF) energy to achieve pulmonary vein isolation (PVI). However, there are many limitations to the current standard of care ablation technologies, and even when PVI is performed at highly experienced centers, reconnected PVs are observed in about 20% of patients [ref]. Additionally, the reliance of these technologies on conductive heating and cooling poses risks to organs or tissue adjacent to the heart which can lead to adverse events such as, atrial-esophageal fistula, pulmonary vein stenosis, phrenic nerve palsy, among others [ref]. Irreversible electroporation (IRE) is a mechanism of inducing cell death via the application of pulsed electric fields (PEF). Pulsed field ablation (PFA) utilizes IRE to selectively destabilize cellular membranes to initiate cell death, resulting in a non-thermal ablation lesion. Interestingly, myocardial tissue has a lower voltage threshold susceptible to PFA when compared to surrounding tissues such as the esophagus, blood vessels, and nerve fibers [ref], therefore reducing risk of damage to these non-cardiac tissues and potentially lowering rates of associated adverse events. In review of the current literature, studies/surveys such as the IMPULSE/PEFCAT/PEFCAT II, PersAFOne, PULSED AF, 5S, and MANIFEST-PF have shown PFA catheters are as safe or safer than other ablation strategies.16-21 Additionally, none of the clinical trials reviewed found PFA catheters to be less safe than the current standard ablation catheters. Each PFA device currently in pre-clinical or clinical investigation are unique in their electrode design, pulse length, pulse number, and voltage. These parameters are critical in developing optimal PFA energy delivery for safe and durable lesions. Thus far, all studies have shown high acute efficacy in achieving PVI and a low rate of recurrent atrial arrhythmias.

With the growing burden of AF on the healthcare system and continued need for increased safety and effectiveness in treatments, the Volt* PFA System has been developed to deliver high-voltage therapy for the safe and effective treatment of symptomatic recurrent AF.

Study objective

The VOLT AF First-in-Human (FIH) study will collect feasibility data to show

that the Volt PFA System functions as intended in a clinical setting and to demonstrate acute safety and effectiveness for the treatment of symptomatic, recurrent paroxysmal atrial fibrillation (PAF) and persistent atrial fibrillation (PersAF).

Study design

.Pre-market, prospective, single-arm, non-randomized, multicenter first-in-human clinical study

Intervention

Pulmonal Vein isolation (PVI) through Pulsed Field ablation (PFA)

Study burden and risks

Extensive risk analysis and risk mitigation plans will be implemented to minimize any residual risk of the Volt* PFA Catheter, Sensor Enabled*, along with the Volt* PFA Generator, Agilis* NxT Steerable Introducer Dual-Reach*, and EnSite* X EP System EnSite* Pulsed Field Ablation Module and EnSite* X IDE Display Workstation to subjects. The risks associated with Abbott*s Volt PFA System are anticipated to be comparable to those associated with the use of other commercially available ablation catheters approved for the treatment of symptomatic recurrent PAF and PersAF. The patients participating in this study are indicated for cardiac ablation for treatment of symptomatic recurrent PAF or PersAF as part of their standard medical management and are subject to the risks associated with these devices.

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 symptomatic PAF or PersAF. Documentation requirements are as follows:
Paroxysmal:
• Physician*s note indicating recurrent self-terminating AF AND
• One electrocardiographically documented PAF episodes within 12 months.
Documented evidence of the PAF episode must either be continuous AF on a 12-lead ECG or include at least 30 seconds of AF from another ECG device.

Persistent: Continuous AF sustained beyond 7 days and less than 1 year that is documented by
• Physician's note, AND either
• 24-hour Holter within 180-days prior to the procedure, showing continuous AF, OR
• Two electrocardiograms (from any form of rhythm monitoring) showing continuous AF:
o that are taken at least 7 days apart but less than 12 months apart
o If electrograms are more than 12 months apart, there must be one or more Sinus Rhythm
recordings in between or within 12 months prior to consent/enrollment
with the most recent electrocardiogram within 180 days of enrollment.
Documented evidence of the AF episode must either be continuous AF on a 12-lead ECG or include at least 30 seconds of AF from another ECG device.

2. Plans to undergo a PVI catheter ablation procedure due to symptomatic PAF or PersAF that is
refractory or intolerant to at least one Class I or III antiarrhythmic drug

3. At least 18 years of age
4. Able and willing to comply with all trial requirements including pre-procedure, post- procedure, and follow-up testing and requirements
5. Informed of the nature of the trial, agreed to its provisions, and has provided written informed consent as approved by the Institutional Review Board/Ethics Committee (IRB/EC) of the respective clinical trial site.

Exclusion criteria

A patient will be excluded from enrollment in the clinical trial if he/she meets any of the following criteria:

1. Previously diagnosed long-standing persistent atrial fibrillation (AF greater than 1 year in duration)
2. Arrhythmia due to reversible causes including thyroid disorders, acute alcohol intoxication, electrolyte imbalance, severe untreated sleep apnea, and other major surgical procedures in the preceding 90 days
3. Participant known to require ablation beyond PVI prior to initiating the index procedure
4. Known presence of cardiac thrombus
5. Left atrial diameter >= 5.5 cm (anteroposterior diameter)
6. Left ventricular ejection fraction < 35% as assessed with echocardiography within 180 days of index procedure
7. New York Heart Association (NYHA) class III or IV heart failure
8. Body mass index > 40 kg/m2
9. Pregnant, nursing, or planning to become pregnant during the clinical investigation follow-up period
10. Patients who have had a ventriculotomy or atriotomy within the preceding 28 days of procedure,
11. Myocardial infarction (MI), acute coronary syndrome, percutaneous coronary intervention (PCI), or valve or coronary bypass grafting surgery within preceding 90 days
12. Unstable angina
13. Stroke or TIA (transient ischemic attack) within the last 90 days
14. Heart disease in which corrective surgery is anticipated within 180 days after procedure

15. History of blood clotting or bleeding abnormalities including thrombocytosis, thrombocytopenia,
bleeding diathesis, or suspected anti-coagulant sate
16. Contraindication to long term anti-thromboembolic therapy
17. Patient unable to receive heparin or an acceptable alternative to achieve adequate
anticoagulation
18. Known sensitivity to contrast media (if needed during the procedure) that cannot be controlled
with pre-medication
19. Previous left atrial surgical or catheter ablation procedure (including LAA closure device)
20. Presence of any condition that precludes appropriate vascular access
21. Severe mitral regurgitation (regurgitant volume >= 60 mL/beat, regurgitant fraction >= 50%, and/or
effective regurgitant orifice area >= 0.40cm2).
22. Previous tricuspid or mitral valve replacement or repair
23. Patients with prosthetic valves
24. Patients with a myxoma
25. Patients with an interatrial baffle or patch as the transseptal puncture could persist and produce
an iatrogenic atrial shunt
26. Stent, constriction, or stenosis in a pulmonary vein
27. Rheumatic heart disease
28. Hypertrophic cardiomyopathy
29. Diagnosed with amyloidosis or atrial amyloidosis
30. Active systemic infection
31. Renal failure requiring dialysis
32. Severe pulmonary disease (e.g., restrictive pulmonary disease, constrictive or chronic
obstructive pulmonary disease) or any other disease or malfunction of the lungs or respiratory
system that produces severe chronic symptoms
33. Presence of an implantable therapeutic cardiac device including permanent pacemaker,
biventricular pacemaker, or any type of implantable cardiac defibrillator (with or without
biventricular pacing function) or planned implant of such a device for any time during the follow-
up period. Presence of an implantable loop recorder is acceptable as long as it is removed prior
to insertion of the investigational device.
34. Presence of an implanted LAA closure device or plans to have an LAA closure device
implanted during the follow-up period
35. Patient is currently participating in another clinical trial or has participated in a clinical trial within

30 days prior to screening that may interfere with this clinical trial without pre-approval from this study Sponsor
36. Unlikely to survive the protocol follow up period of 12 months
37. Presence of other medical, anatomic, comorbid, 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.
38. Individuals without legal authority
39. Individuals unable to read or write

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	7
Type:	Anticipated

Medical products/devices used

Generic name:	Volt PFA system
Registration:	No

Ethics review

Not approved

Date:	31-01-2023

Application type:	First submission
Review commission:	METC NedMec

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
CCMO	NL82553.000.22