Adagio Medical Pulsed Field Ablation (PFA) and Pulsed Field Cryoablation (PFCA) Systems for persistent Atrial Fibrillation (PsAF)

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First-In-Human Clinical Investigation to evaluate the safety and performance of the Adagio Medical PFA and PFCA Systems in the ablation treatment of symptomatic Persistent Atrial Fibrillation (PsAF).

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

Summary

ID

NL-OMON57212

Source
ToetsingOnline

Brief title
PARALLEL

Condition

- Cardiac arrhythmias

Synonym
Arrhythmia; Atrium fibrillation; irregular heartbeat

Research involving
Human

Sponsors and support

Primary sponsor: Adagio Medical, inc.

Source(s) of monetary or material Support: industry. The study is funded by the sponsor;Adagio Medical

Intervention

Keyword: Adagio Medical, PFA, PFCA, PsAF

Outcome measures

Primary outcome

The Primary Endpoint for Safety is an analysis of the proportion of subjects

who are free from device/procedure-related Major Adverse Events (MAEs) that

occur during or following the ablation procedure (7 Days). MAEs include any of

the following:

• Death

• Myocardial infarction

• Persistent diaphragmatic paralysis

• Cardiac perforation/pericardial tamponade

• Stroke/Transient ischemic attack (TIA) or systemic thromboembolism

• Major bleeding requiring transfusion of blood products

• Mitral or tricuspid valve damage

• Symptomatic severe pulmonary vein stenosis (>= 70%)

• Access site complications requiring surgical intervention

• Atrio-esophageal fistula

• Pericarditis requiring medical intervention or prolonged hospitalization.

• Heart block requiring a permanent pacemaker

• Vagal nerve injury with GI dysmotility

• Other serious adverse device effects (SADEs), adjudicated by an independent

DSMB as *probably or definitely related* to the Adagio System

The Primary Procedural Performance Outcome is an analysis of the evidence of procedural electrical isolation of all pulmonary veins, posterior wall, and bidirectional block (if applicable) across all other ablation lines using the study device.

Secondary outcome

Safety

Recording and analysis of all identified serious adverse events (SAEs) and serious adverse device effects (SADEs) through 12 months post-procedure. Events will be adjudicated by an independent Data Safety Monitoring Board (DSMB) for severity and relationship to the Adagio System. Events will be sub-stratified based on time to event as follows:

- Early onset (procedure through 7-days post-ablation)
- Post-procedure (> 7-days through 30-days post-ablation)
- Late onset (>30-days post ablation)

Procedural Performance

- Procedure fluoroscopy time
- Ablation time defined as the total time for energy delivery to achieve PVI, PWI, and CTI or MI
- Total procedure time defined as the time from first venous access to the removal of the last sheath
- The rate of intraprocedural PV reconnection - defined as confirmed conduction

across a PVI line during the 20-minute waiting period to confirm PVI

- Recording of the use of AADs in the follow up period beyond a 90-day blanking period

- Number of repeat ablation within and following the blanking period

One-Year Performance

The one-year performance outcome will be measured as proportion of subjects receiving a single ablation procedure who has freedom from any documented left atrial arrhythmia (AF/AFL/AT) lasting longer than 30 seconds following the Blanking Period (3-months ± 14-days post index ablation) using a continuous 48-hour ECG recording (Holter monitor) through 12 months post-procedure. Patients remaining on AAD at doses less than or equal to those used pre-ablation would also be considered successful.

Study description

Background summary

Atrial fibrillation (AF) remains the most commonly treated sustained arrhythmia affecting approximately 1% to 2% of the general population worldwide. It is a major public health concern in the United States and in 2001, it was reported to be affecting an estimated 2.3 million Americans. By the year 2050 this may reach 12-million. Age adjusted population trending projects 17.9 million people in the European Union will have AF by 2060. AF is associated with a five-fold risk of stroke, a three-fold incidence of congestive heart failure, and higher mortality.
Several factors have been associated with an increased risk of AF. The prevalence of AF increases with age and affects eight to ten percent of patients older than 80 years of age. AF is also more common in males. Data from the Framingham

Heart Study suggest that men are 1.5 times more likely to develop AF than are women after controlling for age and comorbidities. Obesity increases the risk of developing AF. Data from community-based cohorts suggest that obese persons have a 1.5 to 2.3 greater risk of developing AF. Furthermore, obesity increases the likelihood that AF will progress from paroxysmal to permanent AF. Additional factors that have been associated with an increased risk of AF include smoking, hypertension, hyperthyroidism, obstructive sleep apnea, diabetes, myocardial infarction, heart failure, and cardiac surgery.

Atrial fibrillation is currently classified by the duration of the episode documented by ECGs, cardiac rhythm strips, loop recorders or intracardiac electrogram monitoring. The following definitions are used for AF classification:

Paroxysmal AF Defined as AF that terminates spontaneously or with intervention within 7 days of onset.

Persistent AF Defined as continuous AF that is sustained beyond 7 days.

Long-standing Persistent AF Defined as continuous AF of greater than 12 months* duration.

Permanent AF Permanent AF is defined as the presence of AF that is accepted by the patient and physician, and for which no further attempts to restore or maintain sinus rhythm will be undertaken. The term permanent AF represents a therapeutic attitude on the part of the patient and physician rather than an inherent pathophysiological attribute of AF. The term permanent AF should not be used within the context of a rhythm control strategy with antiarrhythmic drug therapy or AF ablation.

The heart*s normal conduction pathway (sinus rhythm) typically begins in the right atrium and proceeds in a single, orderly wave front at rates of 60 to 100 beats per minute. Atrial fibrillation disrupts normal rhythm by creating multiple wave from a rapid ventricular response leading to an irregular pulse as well as diminished cardiac output related to these uncoordinated contractions. Pooling of blood in areas of the atria (i.e. atrial appendage) may allow clots to form and lead to thromboembolic events such as stroke and transient ischemic attacks (TIAs).

Atrial fibrillation is characterized by a chaotic contraction of the atrium in which an electrocardiogram (ECG) recording is necessary to diagnose the arrhythmia. Any arrhythmia that has the ECG characteristics of AF and lasts sufficiently long for a 12-lead ECG to be recorded, or at least 30 seconds on a rhythm strip, should be considered an AF episode. The diagnosis requires an ECG or rhythm strip demonstrating: (1) Irregular RR intervals (in the absence of complete AV block), (2) no distinct P waves on the surface ECG, and (3) an atrial cycle length (when visible) that is usually

variable and less than 200 milliseconds. For many years, three major schools of thought competed to explain the mechanism(s) of AF: multiple random propagating wavelets, focal electrical discharges, and
localized reentrant activity with fibrillatory conduction.
Significant progress has been made in defining the mechanisms of initiation and perpetuation of AF. One of the most
important breakthroughs was the recognition that, in a subset of patients, AF was triggered by a rapidly firing focus and
could be *cured* with a localized catheter ablation procedure. This landmark observation caused the EP community to
refocus their attention on the pulmonary veins (PVs) and the posterior wall of the left atrium (LA), as well as the autonomic
innervation in that region. It also reinforced the concept that the development of AF requires *trigger* and an anatomic or
functional substrate capable of both initiation and perpetuation of AF.
The management of AF involves rate control, rhythm control with antiarrhythmic drugs (AADs), and more recently catheter
ablation. The 2017 HRS/EHRA/ECAS/APHRS/SOLACE expert consensus has stated: *The role of catheter ablation as firstline
therapy, prior to a trial of a Class I or III
antiarrhythmic agent, is an appropriate indication*. The most commonly used catheter ablation approaches to treat AF are
pulmonary vein isolation (PVI) and pulmonary vein antrum isolation (PVAI). Isolation of the pulmonary veins may also be
achieved through wide area circumferential ablation
(WACA). If the pulmonary veins are targeted, complete electrical isolation should be the desired endpoint.
As AF progresses into a more persistent state, additional non-PV targets may be included in the ablation strategy. In a
recent land-mark clinical study, Verma, et al randomized the persistent AF population into three treatment groups.
• PVI
• PVI plus a roof line and a mitral isthmus line
• PVI plus ablation of complex fractionated electrograms
Single treatment efficacy results demonstrated the PVI only group had improved longer-term outcomes although the sample
size was much smaller than the other groups (67 versus 259 versus 263). There was no statistical difference in outcomes
between the latter two groups.
In 2008, Hummel, et al investigated a persistent and long-standing persistent AF population with a treatment strategy that
included PVI plus elimination of fractionated electrograms on the left atrial septum and posterior wall.
A two- treatment efficacy was reported to be 55.8% as measured by a 48-hour Holter at 6-months.

Study objective

First-In-Human Clinical Investigation to evaluate the safety and performance of the Adagio Medical PFA and PFCA Systems in the ablation treatment of symptomatic Persistent Atrial Fibrillation (PsAF).

Study design

A prospective, two-arm, multi-center, randomized, open-label, pre-market, First-in-Human clinical study designed to provide safety and performance data regarding the use of the Adagio PFA and PFCA Systems in the treatment of PsAF.

Intervention

A de novo endocardial ablation of symptomatic, drug-refractory PsAF, followed by clinical follow up visits at discharge, 7 days (phone call), 1 month (phone call), 3 months, 6 months and 12 Months.

Study burden and risks

Patient burden includes additional hospital contacts beyond the standard of care for ablations. Those visits are at 7 days (by phone), 1 month (by phone) and 6 months (at the hospital). There is additional burden for wearing a rhythm monitor to record individual events and for 48-hour recordings at the follow up time points.

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

IC 1. Male or female between the ages of 18 - 80 years
IC 2. Currently scheduled for an ablation of symptomatic persistent (> 7 days) atrial fibrillation within the past year documented by ECG or Continuous Holter monitoring
IC 3. Refractory to at least one class I or III AAD. (Refractory defined as not effective, not tolerated or not desired)
IC 4. Willingness, ability and commitment to participate in baseline and follow-up evaluations for the full length of the study
IC 5. Willingness and ability to give an informed consent

Exclusion criteria

EC 1. In the opinion of the Investigator, any known contraindication to an atrial ablation, TEE, or anticoagulation. Including but not limited to the identification of any atrial thrombus or evidence of sepsis
EC 2. Continuous AF lasting longer than 12-months
EC 3. History of previous left atrial ablation or surgical treatment for AF/AFL/AT
EC 4. AF secondary to electrolyte imbalance, active thyroid disease, or any other reversible or non-cardiac cause
EC 5 Structural heart disease as described below:
a. Left ventricular ejection fraction (LVEF) < 40% based on most recent TTE
b. Left atrial size > 55 mm (parasternal long axis view) documented within 6-months of screening
c. NYHA Class III or IV heart failure documented within the previous 12-months
d. An implanted pacemaker or ICD

e. Previous cardiac surgery, ventriculotomy, or atriotomy (excluding atriotomy for CABG),
f. Previous cardiac valvular surgical or percutaneous procedure, or prosthetic valve
g. Interatrial baffle, closure device, patch, or PFO occluder
h. Presence of a left atrial appendage occlusion device
i. Presence of any pulmonary vein stenting devices
j. Coronary artery bypass graft (CABG) or PTCA procedure within six (6) months prior to procedure
k. Unstable angina or ongoing myocardial ischemia
l. Myocardial infarction within the previous six (6) months prior to procedure
m. Moderate or severe mitral insufficiency or stenosis based on most recent TTE
n. Atrial myxoma
o. Significant congenital anomaly
EC 6. BMI > 40
EC 7. Any previous history of cryoglobulinemia
EC 8. History of blood clotting or bleeding disease
EC 9. History of severe COPD requiring steroid use in the previous 12-months
EC 10. History of severe sleep apnea (AHI > 30) not currently treated with a CPAP machine or other mechanical device
EC 11. Stroke or TIA within the last year.
EC 12. Any prior history or current evidence of hemidiaphragmatic paralysis
EC 13. Pregnant or lactating (current or anticipated during study follow-up
EC 14. Current enrollment in any other study protocol where testing or results from that study may interfere with the procedure or outcome measurements for this study
EC 15. Any other condition such as mental illness, addictive disease, terminal illness with a life expectancy of less than two years, extensive travel away from the research center that may lead to possible inability to comply with the protocol procedures or follow-up.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-10-2022
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	Pulsed Field Ablation System (PFA System) and Pulsed Field Cryoablation System (PFCA)
Registration:	No

Ethics review

Approved WMO Date:	07-07-2022
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-03-2024
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	NCT05408754
CCMO	NL80778.000.22