FARAWAVE™

Pulsed Field Ablation Catheter

FARAPULSE

REF M004PF41M401; M004PF41M402

℞ **ONLY**

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

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REUSE WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific (BSC) representative.

For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

Carefully read all ancillary device instructions prior to use. Observe all contraindications, warnings and precautions noted in these instructions. Failure to do so may result in patient complications.

DEVICE DESCRIPTION

The FARAWAVE Pulsed Field Ablation (PFA) Catheter (henceforth referred to as the FARAWAVE Catheter) is a component of the FARAPULSE PFA System.

The FARAWAVE Catheter is an over-the-wire, multi-electrode catheter designed to deliver PFA energy to the distal section for cardiac ablation. The FARAWAVE Catheter distal section consists of five splines with four electrodes located on each spline, twenty electrodes total.

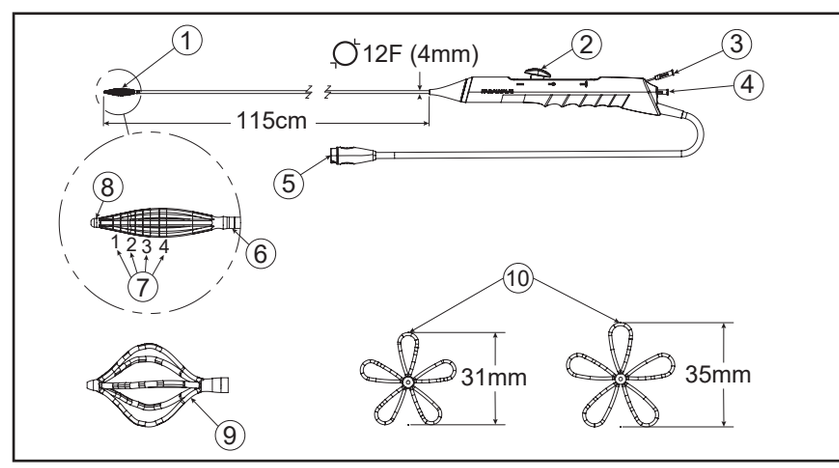


Figure 1. FARAWAVE Catheter

(1) Distal splines (2) Deployment mechanism (3) Flush port (4) Guidewire hub (5) Cable connector (6) Radiopaque marker (7) Four electrodes on five splines (8) Radiopaque tip (9) Partial ("basket") deployment (10) Full ("flower") deployment

The FARAWAVE Catheter handle features a deployment mechanism that enables the ability to deploy the distal section into multiple configurations, where the partially deployed configuration is a "basket" shape and the fully deployed configuration is a "flower" shape. The symbols on the FARAWAVE Catheter handle indicate each configuration.

Table 1. FARAWAVE Catheter Configurations

Symbol	Configuration
	Undeployed
	Partially deployed ("basket")
	Fully deployed ("flower")

The FARAWAVE Catheter is a 12F catheter and is compatible with the FARADRIVE Steerable Sheath (henceforth referred to as the FARADRIVE Sheath). The FARAWAVE Catheter is available in two sizes, 31 mm and 35 mm, representative of the fully deployed diameter.

For ablation, the FARAWAVE Catheter is designed to be used with the FARASTAR Catheter Connection Cable and FARASTAR Generator.

Contents

One (1) sterile FARAWAVE Catheter

Materials

Contains Cobalt; CAS No 7440-48-4; EC No. 231-158-0. Defined as a 1B according to the European Commission in a concentration above 0.1% weight by weight.

Note: This device is made with a metal alloy which contains cobalt. Current scientific evidence supports that metal alloys containing cobalt used in medical devices do not cause an increased risk of cancer or adverse reproductive effects.

Non-pyrogenic

This device meets pyrogen limit specifications for all patient-contacting parts.

INTENDED USE/INDICATIONS FOR USE

The FARAWAVE Catheter is indicated for:

- the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).
- the isolation of pulmonary veins and the posterior wall in the treatment of drug-refractory, symptomatic Persistent Atrial Fibrillation (episode duration less than one year).

Intended Patient Population

The FARAPULSE PFA System is intended for adult cardiac arrhythmia patients who are age 18 or older.

CONTRAINDICATIONS

The FARAWAVE Catheter is contraindicated for use:

- in patients with active systemic infection;
- in patients with a mechanical prosthetic heart valve through which the catheter must pass;
- in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation;
- in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation;
- in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require

catheter insertion from the femoral approach;

- in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels);
- via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch.

WARNINGS

- If the visibility of the EP catheter is compromised for any reason, the user should stop and not resume ablation therapy until catheter visibility is established in order to prevent patient injuries such as perforation, heart block and injury to adjacent structures.
- Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology, in the techniques of mapping and ablation, and in the specific approach to be used, in a fully equipped electrophysiology lab. Device specific physician in-service training is made available by the manufacturer.
- Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboembolism if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post procedure according to the institution's standards to minimize bleeding and thromboembolic complications.
- Carefully read all equipment and ancillary device instructions required for the procedure prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient complications.
- Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury.
- Before using, inspect the FARAWAVE Catheter for any defects or physical damage, including electrical insulation on the cables and the catheter shaft that, if used, may cause patient and/or user injury. Do not use defective or damaged devices. Replace damaged equipment if necessary. No modification of this equipment is allowed.
- Electromagnetic Interference (EMI) from any source during normal operation may adversely affect the visualization and tracking of the catheter during the procedure, which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Please reference the FARASTAR capital equipment IFU for instructions for maintaining basic safety and essential performance with regard to electromagnetic disturbances.
- Use of the FARAWAVE Catheter with generators other than a compatible BSC PFA Generator can lead to unexpected energy delivery resulting in either insufficient ablation treatment or over-delivery of energy leading to possible patient hazardous events such as thrombus formation, tissue damage, etc.
- Patients undergoing ablation are at risk for complete AV block which requires the implantation of a temporary and/or permanent pacemaker.
- When the catheter is in the patient, the patient and/or the catheter connector should not come in contact with grounded metal surfaces to minimize the potential for electrical shock.
- Ensure that the cable/catheter connection remains dry throughout the procedure in order to prevent electric shock or other patient injuries as well as to prevent loss of device function.
- Fibrin may accumulate in or on the sheath/catheter assembly during the procedure. Aspirate when removing the catheter.
- In the presence of anticoagulation, there may be an increased risk of bleeding from all causes.
- Electrical recording or stimulation equipment must be isolated. Current leakage from any electrical equipment that is connected to the patient must not exceed 10 microamps for intracardiac electrodes.
- Care must be taken to ensure that any equipment used in connection with the FARAWAVE Catheter be type CF, be defibrillation proof, meet IEC 60601-1 electrical safety requirements, and comply with all local regulatory

requirements for specified intended use to reduce the potential risk of inadvertent electrical shock.

- Do not directly touch the patient or any conductive surface when ablation energy is being delivered to prevent the risk of electric shock. Contact with patient or a conductive surface during energy delivery could result in discomfort.
- Stimulation of cardiac tissues caused by pacing stimulus and/or ablation energy may lead to inadvertent induction of arrhythmias. These arrhythmias may require defibrillation that could also result in skin burns.
- Warnings for patients with implantable pacemakers (PPMs) and Implantable Cardioverter Defibrillators (ICDs):
    - PPMs, ICDs, and leads can be adversely affected by ablation energy. It is important to refer to the device manufacturer's instruction for use prior to performing ablation procedures.
    - Do not apply ablation energy directly to a lead or to tissue immediately in contact with a lead because it could potentially damage the lead or lead function.
    - Temporarily reprogram the pacemaker or defibrillator per the manufacturer guidelines during ablation. The device could be damaged by the ablation procedure. Interrogate the device fully after the ablation per the manufacturer guidelines and reprogram to preoperative sensing and pacing parameters.
    - Program the ICD Tachy therapy to "Off" to prevent inappropriate shock and/or possible damage to the device from the ablation procedure. Remember to turn Tachy Therapy to "On" once ablation is complete.
    - Have temporary external sources of pacing and defibrillation available.
    - Perform a complete analysis of the implanted device function after ablation.
    - Fluoroscopic or appropriate imaging guidance and care must be taken during catheter advancement, manipulation, and withdrawal to avoid lead dislodgement.
    - Monitor pre- and post-measurements for sensing and pacing thresholds and impedances to determine the integrity of the lead-patient function.
- Ablation in contact with any other electrodes alters the function of the catheter and can lead to embolism.
- At no time should a FARAWAVE Catheter be advanced, withdrawn, rotated, deployed or undeployed when resistance is felt, without determining the cause. Valve damage, vascular and/or cardiac perforation is a risk with any intracardiac catheter.
- Catheter entrapment within the heart or blood vessels is a possible complication of cardiac ablation procedures. The potential for catheter entrapment may be increased when the catheter is over torqued and/or positioned in the chordae tendineae. The occurrence of this complication may necessitate surgical intervention and/or repair of injured tissue and/or valve damage.
- Do not use the FARAWAVE Catheter in the proximity of Magnetic Resonance Imaging (MRI) equipment because the MRI equipment may adversely impact the function of a PFA Generator and the ablation system may adversely impact the image quality. This can also lead to loss of visibility during ablation which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Catheter ablation procedures present the potential for significant radiation exposure, which can result in acute radiation injury as well as an increased risk for somatic and genetic effects, to both patients and laboratory staff due to the radiation beam intensity and duration of the fluoroscopic imaging. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Due to radiation exposure during catheter ablation, the safety and effectiveness of this device has not yet been established in pregnant and/or nursing women and pediatric patients.
- There are no data to support the safety and effectiveness of this device in the pediatric population.
- Prior to the procedure, always identify the patient's risk of volume overload. Monitor the patient's fluid balance throughout the procedure and after the procedure to avoid fluid volume overload. Some patients may have factors that reduce their ability to handle the volume overload, making them susceptible to developing pulmonary edema or heart failure during or after the procedure. Patients with congestive heart failure or renal insufficiency, and the elderly are particularly susceptible.
- Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism.
- Excessive curves or kinking of the catheter may damage internal wires and components, including the flush

lumen. This damage may affect mechanical and electrical performance leading to patient injury.

- Do not attempt to bend, kink, or shape the patient-contact portions or flush lumen of the FARAWAVE Catheter. Doing so could cause electrical or mechanical catheter failure resulting in patient injury. Kinking of the flush lumen may compromise flow through the device leading to potential thrombus formation and embolism.
- Use both fluoroscopy, or other visualization techniques such as echocardiography, and intracardiac electrograms to monitor the advancement of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade.
- The FARAWAVE Catheter tip and guidewire move forward during device undeployment. Device deployment and undeployment should be visualized using fluoroscopy. Failure to do so may result in catheter damage and/or patient injury.
- Do not deliver ablation energy with the catheter outside the target site. Ablation Generators can deliver significant electrical energy and may cause patient injury such as arrhythmia and heart block.
- Always verify that the tubing set, catheter, sheath and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing, catheter or sheath can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system.
- Patients undergoing left-sided ablation procedures should be closely monitored during and post procedure for clinical manifestations of myocardial infarction, pulmonary vein injury, nerve damage, and/or embolism.
- Patients undergoing an ablation procedure have the potential for greater anticoagulation and therefore Activated Coagulation Time (ACT) should be monitored closely due to the increased risk for bleeding/ hemorrhage and/or embolism.
- Patients with hemodynamic instability or cardiogenic shock are at increased risk for life-threatening adverse events and ablation must be done with extreme caution.
- The FARAWAVE Catheter is not intended to be used for internal cardioversion. Doing so may result in perforation, arrhythmias, embolism, thrombus and/or patient death.
- Inspect irrigation saline for air bubbles and remove any air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause embolism.
- If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, there should be a low threshold to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/or thrombus in the left atrial appendage.
- Guiding catheters and/or long introducer sheaths present the potential for thromboembolic events. Pre-flush and maintain lumen patency with heparinized intravenous infusion.
- Do not wipe this catheter with organic solvents such as alcohol or immerse the handle and/or cable connector in fluids. This may result in electrical or mechanical catheter failures. It may also result in an allergic reaction from the patient.
- Pre-procedural anticoagulation therapy is at the discretion of the physician. However, patients with a history of thromboembolic events may require therapeutic anticoagulation therapy, pre-, during and post-ablation to reduce the incidence of major complications. Peri-procedural anticoagulation therapy is recommended for patients undergoing left-sided and transseptal cardiac procedures and should be considered for selected patients undergoing right-sided procedures.
- The safety and/or efficacy of epicardial use of the FARAWAVE Catheter has not been evaluated in a clinical trial.
- Care should be used during multiple sheath/catheter exchanges through the transseptal puncture to avoid causing a residual atrial septal defect that would require repair.
- Do not leave the FARAWAVE Catheter in the patient for more than four (4) hours. Failure to remove the device before four hours after first insertion could result in formation of thrombus with increased thromboembolic risk.
- Use of the FARAWAVE Catheter with delivery devices other than the FARADRIVE Sheath can result in poor access to endocardial locations, inefficient ablation delivery and inadequate procedural outcomes.
- Cardiac ablation has the potential of causing unintended myocardial injury. Clinical indications of myocardial ischemia should be closely monitored during the procedure (e.g., ECG changes).
- The FARAWAVE Catheter has not been studied clinically for ablation in the mitral isthmus or cavotricuspid isthmus areas. Ablations in areas adjacent to coronary arteries may lead to coronary artery spasm and/or injury,

and the resulting myocardial injury can be fatal.

- Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.
- When positioning on cardiac structures, the guidewire should be retracted to prevent cardiac perforation or tissue damage. Ensure the tip of the device is not against tissue prior to advancing or retracting the guidewire to prevent cardiac perforation or tissue damage.
- The risk of igniting flammable gases or other materials is potential outcome of ablation procedures. Precautions must be taken to restrict flammable materials from the electrosurgical suite.
- Take care when manipulating the guidewire to prevent cardiac or vessel trauma.
- To avoid cardiac damage, do not use excessive force when manipulating the catheter in vivo. Specifically, use caution when maneuvering while undeployed. Note that mapping and recording data do not require the use of force on the tissue.
- Minimize catheter exchanges and always advance and withdraw components through the valve slowly to minimize the vacuum created during withdrawal and to reduce the risk of air embolism. Follow advancement or withdrawal of catheters with appropriate aspiration and flushing according to institutional standards or consensus statements.
- Instruct users with co-implanted devices to refer to ancillary device labeling as well as the manufacturer of the ancillary device for recommended compatibility and settings. When ablating in proximity to metallic devices, arcing may occur which could lead to bubble formation, cardiac trauma, and/or damage to the devices.
- Use caution when advancing, retracting or otherwise manipulating system components to avoid damaging tissue or vessels or interfering with previously implanted medical devices.
- When advancing or undeploying the FARAWAVE catheter, do not retract the guidewire simultaneously. If resistance is felt during retraction of the guidewire, do not continue to retract the guidewire until cause of resistance is determined as this may result in cardiac trauma. If resistance is felt, it may be necessary to advance guidewire under imaging guidance before continuing to retract.
- Ensure that the guidewire is not contacting ablation electrodes prior to starting ablation to prevent inappropriate energy delivery.
- Always un-deploy the catheter and withdraw the catheter into the sheath before removing the catheter from the Left Atrium (LA). Deploying the catheter in the septal puncture site or crossing the septum while the catheter is unsheathed or deployed may cause serious atrial septal defects or other cardiac and vessel trauma. Use visualization (such as fluoroscopy) to verify undeployment.
- Avoid deploying the catheter in constrained parts of the anatomy to prevent cardiac trauma or damage to the device.
- Prior to starting ablation verify that the catheter has been positioned and deployed correctly to prevent inappropriate application of ablation energy.
- Do not deploy the catheter while the distal end is inside the sheath as it could lead to catheter damage which may result in patient harm.
- Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed in the Operational Instructions section, regardless of absence of intracardiac signal.
- Operation of the FARAPULSE PFA System may cause transient intravascular hemolysis, which may manifest as hemoglobinuria. In order to reduce the risk of clinical sequelae of intravascular hemolysis, it is recommended to adhere to the nominal workflow per the IFU. Consider the application of additional ablations per physician judgment taking into account patient condition including hydration status, anatomy, and available clinical evidence with FARAPULSE PFA System. Evaluate the patient's risk tolerance for hemoglobinemia and related sequelae prior to the procedure. Consider hydration prior to, during, and post-procedure.
- Potential biohazard after use. Handle and dispose of in accordance with applicable regulations.

PRECAUTIONS

- Do not attempt to use with devices, including guidewires, larger than the delivery lumen diameter specified on the package label.
- Care must be taken to ensure all luer fittings are secure to prevent leaking.
- It is essential that a cardiac defibrillator with paddles connected is readily available in the procedure room for use if Ventricular Fibrillation is noted subsequent to ablation.
- Catheter deployment and undeployment should occur under imaging guidance. Catheter may be fully deployed or undeployed even though the slider switch is not fully engaged. Failure to monitor deployment may result in catheter damage and need for catheter exchange.
- Device deployment friction is increased when attempting to deploy the device when the catheter shaft is bent. FARAWAVE Catheter deployment should always occur with the catheter shaft as straight as possible.
- Do not apply excessive force to the deployment mechanism when deploying the catheter as doing so may damage the catheter.
- Avoid allowing the distal end of the catheter to be put into an acute bend, particularly when advancing the catheter beyond the sheath or deploying the catheter. A catheter exchange may be necessary if the catheter deploys improperly.

ADVERSE EVENTS

Potential adverse events associated with use of the FARAWAVE Catheter includes, but are not limited to:

- Pain or discomfort, for example:
  - Angina
  - Chest pain
  - Non-cardiovascular pain
- Cardiac arrest
- Death
- Electric shock
- Hypotension
- Infection/inflammation/exposure to biohazardous material
- Pulmonary edema/heart failure/pleural effusion
- Renal failure/insufficiency
- Respiratory distress/insufficiency/dyspnea
- Arrhythmia (new or exacerbated)
  - Conduction pathway injury (for example: heart block, injury to sinus or AV node, etc.)
- Nerve injury, for example:
  - Phrenic nerve injury
  - Vagal nerve injury
- Gastrointestinal disorders
- Vessel trauma, including:
  - Perforation
  - Dissection
  - Coronary artery injury
  - Vasospasm
  - Occlusion
  - Hemothorax
- Cardiac trauma, for example:
  - Cardiac perforation/cardiac tamponade/pericardial effusion
  - Valvular damage
  - Stiff left atrial syndrome

- Injury related to tissue damage and/or adjacent structures, for example:
  - Esophageal injury
  - Pulmonary injury
  - Catheter entrapment
  - Physical trauma
- Fistula, for example:
  - Atrio-esophageal fistula
  - Bronchopericardial fistula
- PV stenosis and its symptoms, for example:
  - Cough
  - Shortness of breath, fatigue
  - Hemoptysis
- Surgical and access site complications, for example:
  - Hematoma/seroma
  - AV fistula
  - Bleeding
  - Pseudoaneurysm
  - Pneumothorax
  - Residual atrial septal defect
- Thrombus/thrombosis
- Muscle spasm
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
  - Cerebrovascular Accident (CVA)/stroke
  - Transient Ischemic Attack (TIA)
  - Myocardial infarction
  - Neurological impairment and its symptoms, for example:
    - Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment
  - Pulmonary embolism
  - Peripheral embolism
  - Asymptomatic cerebral embolism
- Hemolysis
- Procedural related side effects, for example:
  - Allergic reaction (including anaphylaxis)
  - Genitourinary complication
  - Side effects related to medication or anesthesia
  - Radiation injury/tissue burn
  - Vasovagal response
  - Fluid volume overload

The potential adverse events may be related to the ablation catheter(s) and/or the interventional procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death.

CLINICAL STUDIES

ADVENT Clinical Study

Study Title	The ADVENT Trial – A Prospective Randomized Pivotal Trial of the FARAPULSE Pulsed Field Ablation System Compared with Standard of Care Ablation in Patients with Paroxysmal Atrial Fibrillation
Number of Centers	30 sites in the United States
Number of Subjects	706 enrollments, including 80-roll-in subjects and 626 randomized subjects (313 Pulsed Field and 313 Thermal [171 Radiofrequency (RFA) ablation, 142 Cryoballoon (CBA)]). 19 subjects withdrew prior to the procedure resulting in 607 modified-intent-to-treat (MITT) subjects (305 Pulsed Field and 302 Thermal [167 RF ablation and 135 CBA]).

Objective

The primary objective of the ADVENT Trial was to establish valid scientific evidence that endocardial ablation using the FARAPULSE Pulsed Field Ablation System is both safe and effective for treating patients with drug-resistant, recurrent, symptomatic paroxysmal atrial fibrillation (PAF).

Design, Scope, and Methods

The ADVENT Trial was a prospective, Bayesian adaptive, multi-center, 1:1 randomized, blinded, non-inferiority safety and effectiveness pivotal study comparing the FARAPULSE Pulsed Field Ablation System with thermal ablation (using either force-sensing RFA catheters or CBA catheters) for the treatment of patients with drug-resistant, recurrent, symptomatic PAF. All subjects who met the eligibility criteria, signed the informed consent, and underwent the Index Procedure were followed for 12 months post-ablation with weekly event monitoring beginning on Day 90, and 72-hour Holter monitoring at Months 6 and 12. Clinical follow-up at Days 7, 30, 90, Month 6 and Month 12 were performed to determine any occurrence of adverse events or arrhythmia recurrence.

Endpoints

Primary Safety Endpoint

The primary safety endpoint was the Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device- or procedure-related SAEs as adjudicated by the Clinical Events Committee (CEC) according to the protocol-specified definitions.

Early onset

Any of the following with an Onset Date within 7 days of the Index / Rescheduled Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation
- Pericarditis
- Pulmonary edema
- Vascular access complications
- Heart block
- Gastric motility/pyloric spasm disorders

Late onset

Either of the following with an Onset Date any time through the completion of 12-month follow-up visit:

- Pulmonary Vein Stenosis
- Atrio-esophageal fistula

Hypothesis

The analysis of the primary safety endpoint was a test of non-inferiority of the event rate at 12 months using a non-inferiority margin of 8%. The null and alternative hypotheses are presented below for primary safety:

$H_0: Q_T \geq Q_C + 0.08$ versus $H_A: Q_T < Q_C + 0.08$

where QT is the CSE proportion in the Pulsed Field (Treatment) Group and QC is the CSE proportion in the Thermal (Control) Group. The differences in the proportion of subjects with 1 or more CSE events between the Pulsed Field Group and the Thermal Group will be tested with a Bayesian statistical method and the prior distributions for QT and QC in these calculations are Beta (0.5, 0.5), which is the Jeffreys non-informative prior. QT will be deemed to be non-inferior to QC if it can be established that the posterior probability Pr(HA | data) > Ψsaf, where Ψsaf is a pre-specified threshold value that controls the one-sided type I error rate (under simulation) at level 0.05.

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was Treatment Success in MITT subjects through the Month 12 Assessment, defined as:

1. Acute Procedural Success, defined as demonstration of isolation of all attempted PVs using the randomized treatment during the first ablation procedure as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing and
2. Chronic Success, defined as freedom from:
   a. Use of a non-randomized treatment modality for PVI at the Index Procedure and
   b. After the Blanking Period, occurrence of any detectable atrial fibrillation (AF), atrial flutter (AFL) or atrial tachycardia (AT)[1], any cardioversion for AF, AFL or AT, use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT and
   c. At any time, re-ablation for AF, AFL or AT (other than for CTI-dependent flutter) or use of amiodarone, except intra-procedurally to control an arrhythmia

Hypothesis

The primary effectiveness endpoint for this study was Treatment Success, which will be analyzed as a test of non-inferiority of the event rate at 12 months using a non-inferiority margin of 15%. The null and alternative hypotheses are:

$H_0: P_T \leq P_C - 0.15$ versus $H_A: P_T > P_C - 0.15$

where PT is the Treatment Success rate at 12 months in the Pulsed Field Group and PC is the Treatment Success rate at 12 months in the Thermal (Control) Group.

This study was designed using Bayesian statistical techniques and the prior distributions for PT and PC in these calculations are Beta (0.5, 0.5), which is the Jeffreys non-informative prior. PT will be deemed to be non-inferior to PC if it can be established that the posterior probability Pr(HA | data) > Ψeff, where Ψeff is a pre-specified threshold value that controls the one-sided type I error rate (under simulation) at level 0.05.

Subject Accountability

All subjects who signed and dated the Informed Consent Form were considered enrolled in the study. Subjects were classified as either Roll-In or Randomized:

- **Roll-In Subject** – To help facilitate Investigators' familiarity with the new investigational system and avoid learning curve bias, the first 1-3 subjects at each site were enrolled as Roll-In subjects. Data from Roll-In subjects are not included in the endpoint analyses or results presented.
- **Randomized Subject** – Once roll-in requirements were satisfied, all subsequent subjects enrolled were randomized 1:1 to receive either Pulsed Field ablation or Thermal (control) ablation. Thermal control modality (RFA or CBA) was determined at the site level. Subject classification was as follows:
  - **Intent-to-Treat (ITT)** – Enrolled subjects randomized to either the Pulsed Field group or Thermal group.
  - **Modified Intent-to-Treat (MITT)** – ITT subjects who received any energy delivery for pulmonary vein isolation (PVI) with the randomized ablation catheter the Index Procedure.

1 Detectable AF, AFL or AT is an episode of AF, AFL or AT which is permanently recorded for review, contains at least 30 seconds of continuous interpretable signal, includes symptomatic and asymptomatic episodes, and excludes CTI isthmus-dependent AFL when the mechanism is confirmed electrophysiologically

A total of 706 subjects were enrolled in the study, including 80 Roll-In subjects and 626 Randomized subjects, 313 in the Pulsed Field Group and 313 in the Thermal Group (171 RFA, 142 CBA). Nineteen (19) subjects (8 PFA, 11 Thermal) exited the study prior to undergoing the Index Procedure ablation, resulting in 607 Randomized subjects in the MITT cohort (305 Pulsed Field, 302 Thermal [167 RFA and 135 CBA]). Of the 607 MITT subjects, 583 (96.0%) completed the 12-month follow-up (293 PFA subjects and 290 Thermal subjects), with the 24 early exits equally represented across the groups (12 Pulsed Field, 12 Thermal).

Study Population Demographics, Baseline Parameters, and Visit Compliance

Effective randomization was verified by comparing the groups on basic demographic data, assessments of AF status, and multiple cardiovascular parameters. Key baseline comparators for the MITT subjects are presented in Table 2 and Table 3. While there were a few statistical differences between the Pulsed Field and Thermal groups, commonly seen when multiple comparisons are performed, none were clinically significant.

Table 2. Baseline Demographics and Arrhythmia History – MITT Subjects

Baseline Perimeter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[1]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
Female	34.6 (210/607)	33.8 (103/305)	[-9.2, 5.9]	35.4 (107/302)	32.9 (55/167)	38.5 (52/135)
Male	65.4 (397/607)	66.2 (202/305)		64.6 (195/302)	67.1 (112/167)	61.5 (83/135)
Hispanic or Latino	1.8 (11/607)	2.6 (8/305)	[-0.5, 4.0]	1.0 (3/302)	1.2 (2/167)	0.7 (1/135)
White	91.9 (558/607)	93.8 (286/305)	[-0.6, 8.1]	90.1 (272/302)	89.8 (150/167)	90.4 (122/135)
Black/African American	2.5 (15/607)	1.3 (4/305)	[-5.0, 0.1]	3.6 (11/302)	4.2 (7/167)	3.0 (4/135)
Asian	1.8 (11/607)	2.0 (6/305)	[-1.9, 2.6]	1.7 (5/302)	1.2 (2/167)	2.2 (3/135)
American Indian or Alaska Native	0.2 (1/607)	0.0 (0/305)	[-1.4, 0.5]	0.3 (1/302)	0.6 (1/167)	0.0 (0/135)
Native Hawaiian or other Pacific Islander	0.5 (3/607)	0.3 (1/305)	[-1.7, 0.9]	0.7 (2/302)	1.2 (2/167)	0.0 (0/135)
Race Unknown	1.5 (9/607)	0.7 (2/305)	[-3.8, 0.2]	2.3 (7/302)	1.8 (3/167)	3.0 (4/135)
Race Not Specified	1.6 (10/607)	2.0 (6/305)	[-1.5, 2.8]	1.3 (4/302)	1.2 (2/167)	1.5 (2/135)
Typical Atrial Flutter	30.1 (183/607)	27.2 (83/305)	[-13.1, 1.4]	33.1 (100/302)	42.5 (71/167)	21.5 (29/135)
Other SVT	14.0 (85/607)	11.8 (36/305)	[-10.0, 1.1]	16.2 (49/302)	21.0 (35/167)	10.4 (14/135)
Previous RA Ablation	3.9 (22/562)	3.5 (10/283)	[-4.1, 2.5]	4.3 (12/279)	5.0 (8/161)	3.4 (4/118)

Note 1: Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors.

Table 3. Baseline Demographics and Medical History – MITT Subjects

Baseline Perimeter	Total Subjects Mean (N) Min, Max	Pulsed Field Subjects Mean (N) Min, Max	95% BCI[1]	Thermal Subjects Mean (N) Min, Max	RFA Subjects Mean (N) Min, Max	CBA Subjects Mean (N) Min, Max
Age (years)	62.4 (607) 30, 75	62.4 (305) 36, 75	[-1.5, 1.3]	62.5 (302) 30, 75	62.5 (167) 42, 75	62.4 (135) 30, 75
Height (cm)	175.7 (607) 147, 201	175.9 (305) 147, 198	[-1.0, 2.2]	175.4 (302) 149, 201	176.3 (167) 149, 201	174.2 (135) 149, 196
Weight (kg)	88.7 (607) 45.4, 145.6	87.9 (305) 45.4, 137.9	[-4.5, 1.1]	89.6 (302) 45.6, 145.6	89.0 (167) 45.6, 136	90.3 (135) 47.6, 145.6
BMI	28.7 (607) 15, 47.2	28.3 (305) 15, 41.6	[-1.45, 0.05]	29.0 (302) 17.7, 47.2	28.5 (167) 17.7, 47.2	29.6 (135) 18.6, 40
LVEF (%)	60.1 (600) 40, 78	60.5 (300) 40, 78	[-0.1, 1.9]	59.6 (300) 40, 77	60.6 (167) 40, 77	58.4 (133) 44, 75
Left Atrial Diameter (mm)	39.2 (607) 23, 55	38.8 (305) 23, 55	[-1.6, 0.2]	39.6 (302) 24, 54	39.3 (167) 24, 53	40.0 (135) 25, 54
Years since first AF diagnosis	3.6 (607) 0, 51.55	3.8 (305) 0, 51.55	[-0.4, 1.4]	3.3 (302) 0, 36.19	3.5 (167) 0, 21.65	3.1 (135) 0, 36.19

Baseline Perimeter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[2]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
CAD	13.7 (83/607)	10.5 (32/305)	[-11.9, -0.9]	16.9 (51/302)	17.4 (29/167)	16.3 (22/135)
Diabetes	10.7 (65/607)	10.8 (33/305)	[-4.7, 5.2]	10.6 (32/302)	11.4 (19/167)	9.6 (13/135)
CHF: NYHA Class I or II	19.4 (118/607)	19.3 (59/305)	[-6.5, 6.1]	19.5 (59/302)	18.6 (31/167)	20.7 (28/135)
Sleep Apnea	27.8 (169/607)	26.6 (81/305)	[-9.7, 4.6]	29.1 (88/302)	28.7 (48/167)	29.6 (40/135)
Using CPAP	77.5 (131/169)	71.6 (58/81)	[-23.8, 1.2]	83.0 (73/88)	79.2 (38/48)	87.5 (35/40)
CHA_2DS_2-VASc Score	1.7 (606) 0, 6	1.7 (304) 0, 6	[-0.2, 0.2]	1.7 (302) 0, 6	1.8 (167) 0, 5	1.6 (135) 0, 6

Note 1: Bayesian credible interval for the difference in means, using uniform priors on (μ, log(σ)) scale.
Note 2: Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors.

Follow-up visit compliance (pre-discharge, Day 7, Day 90, Month 6, and Month 12) was high and similar across both treatment groups with an overall compliance rate of 99.3% in the Pulsed Field group (1800/1813) and 99.3% (1786/1799) in the Thermal group. Post-ablation rhythm monitoring for the MITT cohort included symptomatic and weekly event monitor transmissions during the evaluation period, 12-lead ECGs at Day 90 and 12 months, and 72-Hour Holter monitors at 6-months and 12-months post-Index Procedure. Overall rhythm monitoring compliance across all assessment methods was 70.0% (71.3% Pulsed Field and 68.7% Thermal).

Procedural Durations

The duration of clinically relevant portions of each Index Procedure were recorded and compared descriptively. Procedure time (mean 105.8 versus 123.1 minutes), LA dwell time (mean 59.4 versus 83.7 minutes), total ablation time (mean 29.2 versus 50.0 minutes), and pre-ablation mapping time (mean 3.8 versus 6.2 minutes) were all significantly different and shorter in the Pulsed Field group as compared to the Thermal group. Fluoroscopy time was longer

in the Pulsed Field group (mean 21.1 versus 13.9 minutes), as many thermal procedures have shifted to fluoroless procedures, which is further enabled by the integrated mapping system technologies that were used. Procedure times were inclusive of the protocol-required 20-minute wait, CTI ablation time, and any additional ablation, if performed.

Results

Primary Safety Endpoint

The primary safety endpoint was the CSE defined as the proportion of MITT subjects with one or more pre-specified device- or procedure-related SAEs adjudicated by the ADVENT Clinical Events Committee. The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a Bayesian test of non-inferiority of the CSE rate at 12 months using a non-inferiority margin of 8%.

In Pulsed Field MITT subjects, six (6) subjects experienced one or more CSE events; the estimated incidence was 2.1% (posterior mean). In Thermal MITT subjects, four (4) subjects experienced one or more CSE events; the estimated incidence was 1.5% (posterior mean).

The ADVENT Trial met the success criterion for the primary safety endpoint. The probability of a Pulsed Field MITT subject having one or more CSE events was non-inferior to the probability of a Thermal MITT subject having one or more CSE events using a non-inferiority margin of 8%: the posterior probability of non-inferiority was >0.999, which exceeded the prespecified threshold of 0.966 (Table 4).

Table 4. Primary Safety Endpoint – MITT Subjects

Primary Safety Endpoint	Subjects with Events (N) Incidence (%) 95% BCI[1]		Difference (%) 95% BCI[2]	Posterior Probability of Non-Inferiority (δ = 8%)[3]
	Pulsed Field Group N = 305	Thermal Group N = 302		
MITT Subjects with one or more CSE events	6 2.1 [0.8, 4.0]	4 1.5 [0.4, 3.1]	0.6 [-1.5, 2.8]	> 0.999

Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.
Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.
Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

The components of the CSE Events were analyzed as separate outcomes in Table 5. Six (6) Pulsed Field subjects experienced a CSE, of the following types: 1 death, 1 TIA, 2 cardiac tamponade/ perforation, 1 pericarditis, 1 pulmonary edema, and 1 vascular access complication. One subject in the Pulsed Field group experienced two events (death and cardiac tamponade/perforation). Four (4) subjects in Thermal group experience a CSE: 1 stroke, 1 pulmonary edema, and 2 vascular access complications. All CSEs in the Thermal group occurred in RFA subjects.

Table 5. Proportion of MITT Subjects with One or More CSE Events by Event Type

MITT Subjects with One or More CSE Events by Event Type	Pulsed Field Group[1] % (n / N)	Thermal Group % (n / N)
Any CSE Event	**2.0 (6/305)**	**1.3 (4/302)**
Death	0.3 (1/305)	0.0 (0/302)
Myocardial infarction	0.0 (0/305)	0.0 (0/302)
Persistent phrenic nerve palsy	0.0 (0/305)	0.0 (0/302)
Stroke	0.0 (0/305)	0.3 (1/302)
TIA	0.3 (1/305)	0.0 (0/302)
Peripheral organ thromboembolism	0.0 (0/305)	0.0 (0/302)
Cardiac tamponade or perforation	0.7 (2/305)	0.0 (0/302)
Pericarditis	0.3 (1/305)	0.0 (0/302)
Pulmonary edema	0.3 (1/305)	0.3 (1/302)
Vascular access complication	0.3 (1/305)	0.7 (2/302)

MITT Subjects with One or More CSE Events by Event Type	Pulsed Field Group[1] % (n / N)	Thermal Group % (n / N)
Heart block	0.0 (0/305)	0.0 (0/302)
Gastric motility/ pyloric spasm	0.0 (0/305)	0.0 (0/302)
Pulmonary vein stenosis	0.0 (0/305)	0.0 (0/302)
Atrio-esophageal fistula	0.0 (0/305)	0.0 (0/302)

Abbreviations: n = number of subjects with event, N = number of evaluable subjects.

Note 1: PFA Subject 109-017 has event meeting the CSE definition for both death and cardiac tamponade/perforation and is included in event counts for both CSE events

Secondary Safety Endpoint

The secondary safety endpoint was Aggregate PV Cross-Sectional Area, defined as the paired difference in the computed Aggregate PV Cross-Sectional Area between baseline and 3 months in MITT subjects. This was compared between randomization groups, regardless of re-ablation with any second energy modality. The within-subject changes in the Aggregate PV Cross-Sectional Area from baseline to Day 90 were tested between the Pulsed Field and Thermal Groups for superiority (less reduction in area) using a Bayesian version of a t-test.

The secondary safety endpoint success criterion for superiority was met. The mean change in PV cross-sectional area in Pulsed Field MITT subject PVs (–0.18 cm^2 or -0.9% of baseline value) was statistically less than the change in Thermal MITT subject PVs (–1.18 cm^2 or -12.0% of baseline value) with an observed posterior probability of >0.999, exceeding the prespecified threshold value of 0.975 (Table 6).

Examination of the change in Aggregate PV Cross-Sectional Area by ablation modality demonstrated that the difference was driven by the large reduction in RFA subjects, who had a mean reduction of 19.5% in Aggregate PV Cross-Sectional Area. Thermal subjects treated with CBA had a 3.3% reduction.

Table 6. Aggregate PV Cross-Sectional Area by Ablation Modality

Aggregate PV Cross-Sectional Area (cm^2)	Interval	Pulsed Field Subjects Mean (N) Min, Max	Thermal Group		
			All Thermal Subjects Mean (N) Min, Max	RFA Subjects Mean (N) Min, Max	CBA Subjects Mean (N) Min, Max
MITT Subjects	Baseline	8.9 (259) 3.7, 15.3	8.9 (255) 4.0, 17.6	9.1 (137) 5.0, 17.6	8.7 (118) 4.0, 15.7
	Day 90	8.7 (259) 4.2, 15.1	7.8 (255) 3.6, 13.5	7.3 (137) 3.6, 12.4	8.3 (118) 3.7, 13.5
	Percent Change	-0.9 (259) -40.7, 65.5	-12.0 (255) -55.2, 44.3	-19.5 (137) -55.2, 16.8	-3.3 (118) -44.5, 44.3
	Change [95% BCI][1]	-0.18 [-0.37, 0.00]	-1.18 [-1.39, -0.97]	-1.86 [-2.12, -1.59]	-0.39 [-0.67, -0.11]
	Posterior Mean of Difference 95% BCI[2]	1.00 [0.72, 1.28]			
	Posterior Probability of Superiority[3]	>0.999			

Note 1: This change is the paired comparisons of the baseline to Day 90 mean values within each treatment group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log(s)) scale

Note 2: This difference is the comparison of the baseline to Day 90 change in per-subject means between PFA and Thermal group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log(σ)) scale.

Note 3: Posterior probability that the change in baseline to Day 90 mean values is larger (less negative) in the Pulsed Field group than the Thermal group, using a Bayesian version of a t-test; uniform priors on (μ, log(σ)) scale.

Additional Safety Information

There were no Unanticipated Adverse Device Effects (UADEs) in the ADVENT Trial.

Summary of Clinical Trial Adverse Events

The following table summarizes the incidence of all major categories of adverse events, comparing the MITT subjects in the Pulsed Field and the Thermal Groups. There were no statistical differences in any adverse events or SAEs, any procedure- or device-related AEs, between the two groups. There were 20 Pulsed Field subjects with one or more procedure-related SAEs compared with 9 Thermal subjects, a statistical difference presented in the table below. The device-related SAEs are all included within the procedure-related numbers.

Table 7. Overview of Adverse Events – MITT Subjects

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	95% BCI[2]	Thermal Subjects (N = 302) n (%) e[1]	RFA Subjects (N = 167) n (%) e[1]	CBA Subjects (N = 135) n (%) e[1]
Any adverse event	390 (64.3%) 1012	189 (62.0%) 487	[-12.2, 3.0]	201 (66.6%) 525	115 (68.9%) 321	86 (63.7%) 204
Any SAE	71 (11.7%) 103	37 (12.1%) 51	[-4.3, 6.0]	34 (11.3%) 52	21 (12.6%) 37	13 (9.6%) 15
Any procedure-related AE	191 (31.5%) 288	97 (31.8%) 147	[-6.7, 8.0]	94 (31.1%) 141	58 (34.7%) 89	36 (26.7%) 52
Any device-related AE	40 (6.6%) 45	21 (6.9%) 22	[-3.4, 4.6]	19 (6.3%) 23	13 (7.8%) 16	6 (4.4%) 7
Any procedure-related SAE	29 (4.8%) 34	20 (6.6%) 23	[0.2, 7.1]	9 (3.0%) 11	7 (4.2%) 9	2 (1.5%) 2
Any device-related SAE	4 (0.7%) 4	4 (1.3%) 4	[0.1, 3.0]	0 (0.0%) 0	0 (0.0%) 0	0 (0.0%) 0

Note 1: N = number of subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Note 2: Bayesian credible interval of the difference in proportions of subjects with one or more events using Beta (0.5, 0.5) priors

Serious Adverse Events

All adverse events reported were screened by the CEC per the protocol requirements and CEC charter. Events reported as serious, and additional events that study monitors or CEC members felt might be serious, were all formally adjudicated by the CEC.

There were 34 device- or procedure-related SAEs reported in 29 subjects (20 Pulsed Field and 9 Thermal). Eleven (11) of the events in ten (10) subjects were the primary safety endpoint events presented previously in the primary safety endpoint results. The remaining 23 events (16 Pulsed Field and 7 Thermal) are summarized in Table 8 below. All of these SAEs were determined to be resolved (21) events or resolving (2 events) by the conclusion of study participation without reported sequelae.

Table 8. Related Serious Adverse Events by Category – MITT Subjects

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	Thermal Subjects (N = 302) n (%) e[1]	95% BCI[2]
Total Device or Procedure Related Serious Adverse Events	**29 (4.8%) 34**	**20 (6.6%) 23**	**9 (3.0%) 11**	**[0.2, 7.1]**
Atrial Flutter	3 (0.5%) 4	2 (0.7%) 3	1 (0.3%) 1	[-1.0, 1.7]
Atypical (Type II) Atrial Flutter	2 (0.3%) 3	1 (0.3%) 2	1 (0.3%) 1	[-1.2, 1.2]
Pseudoaneurysm	3 (0.5%) 3	1 (0.3%) 1	2 (0.7%) 2	[-1.7, 0.9]
Myocardial Perforation With Tamponade	2 (0.3%) 2	2 (0.7%) 2	0 (0.0%) 0	[-0.3, 2.0]
Oozing/Bleeding	2 (0.3%) 2	2 (0.7%) 2	0 (0.0%) 0	[-0.3, 2.0]
Procedure Related Genitourinary	2 (0.3%) 2	1 (0.3%) 1	1 (0.3%) 1	[-1.2, 1.2]
Pulmonary Edema	2 (0.3%) 2	1 (0.3%) 1	1 (0.3%) 1	[-1.2, 1.2]

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	Thermal Subjects (N = 302) n (%) e[1]	95% BCI[2]
Abnormal Lab Values	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Access Site Complication	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Atrial Fibrillation	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Atrial Flutter Not Specified	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Cerebral Vascular Accident	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Conduction Disturbances/Arrhythmia - Other	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
EP/Ablation Other-Multi Organ Failure	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Fistula (Arterial/Venous)	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Intracardiac Thrombus	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Left Atrial (Type II, Atypical) Atrial Flutter	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Pain Cardiovascular (Non-Ischemic)	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Pericarditis	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Procedure Related Hypertension	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Symptomatic Pericardial Effusion	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Systemic Infection	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Transient Ischemic Attack	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]

Note 1: N = number of subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Note 2: Bayesian credible interval of the difference in proportions of subjects with one or more events using Beta (0.5, 0.5) priors

Primary Effectiveness Endpoint

The primary effectiveness endpoint was Treatment Success (Acute Procedural Success and Chronic Success). The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a test of non-inferiority of the Treatment Success rate at 12 months using a non-inferiority margin of 15%.

In Pulsed Field MITT subjects, 204 subjects were Treatment Successes, while 80 subjects experienced Treatment Failures; the remaining 21 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 21 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment Success Rate is 73.3% (calculated as the mean of the posterior distribution).

In Thermal MITT subjects, 194 subjects were Treatment Successes, while 85 subjects experienced Treatment Failures; the remaining 23 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 23 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment Success Rate is 71.3% (calculated as the mean of the posterior distribution).

The ADVENT trial met the success criterion for the primary effectiveness endpoint. The probability of a Pulsed Field MITT subject having Treatment Success was non-inferior to the probability of a Thermal MITT subject having Treatment Success using a non-inferiority margin of 15%: the posterior probability of non-inferiority is >0.999, which exceeded the prespecified threshold of 0.956.

Table 9. Primary Effectiveness Endpoint – MITT Subjects

Primary Effectiveness Endpoint	Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] Incidence (%) 95% BCI[1]		Difference (%) 95% BCI[2]	Posterior Probability of Non-Inferiority (δ = 15%)[3]
	Pulsed Field Group N = 305	Thermal Group N = 302		
MITT Subjects with Treatment Success	204 [21] 73.3 [68.1, 78.1]	194 [23] 71.3 [66.0, 76.3]	2.0 [-5.2, 9.2]	> 0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

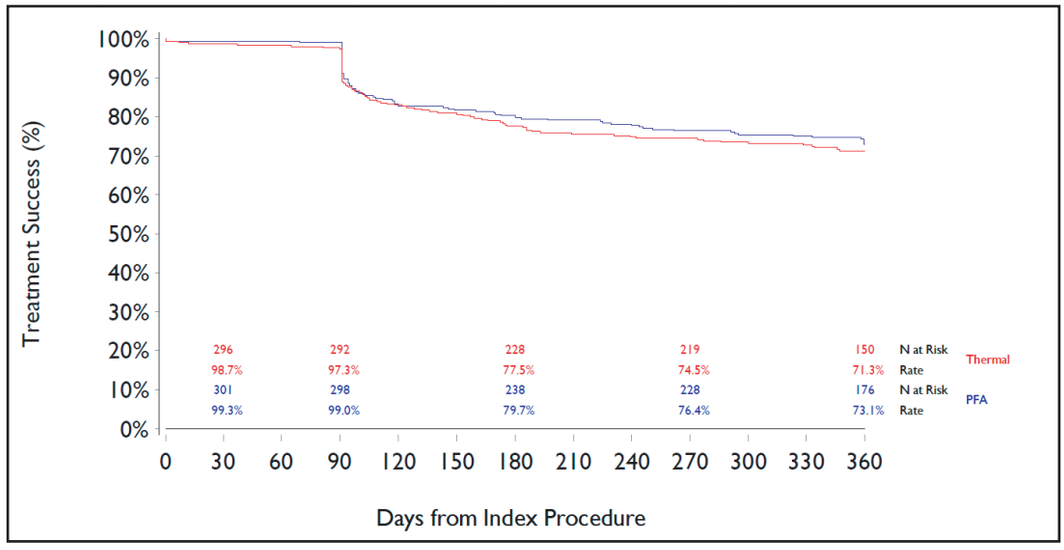
Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.

Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

As a sensitivity analysis, the primary effectiveness endpoint was also assessed via Kaplan-Meier estimates, as shown in Figure 2. The Kaplan-Meier estimate of freedom from failures of the primary effectiveness endpoint at 360 days is 73.1% in the Pulsed Field group and 71.3% in the Thermal group. Although freedom from failures at 360 days differs somewhat from the Treatment Success definition in that 12-month follow-up visits and their associated visit windows are not formally considered, the numerical estimates agree closely: 73.3% for Pulsed Field subjects and 71.3% for Thermal subjects from the pre-specified Bayesian model and 73.1% for Pulsed Field subjects and 71.3% for Thermal subjects from the Kaplan-Meier estimates.

Figure 2. Survival Analysis, Primary Effectiveness Endpoint – MITT Subjects



The mode of the earliest failure of the primary effectiveness endpoint for each MITT subject is detailed in the following table. The data show similar distributions of failure modes for the Pulsed Field and Thermal subjects.

Table 10. Earliest Primary Effectiveness Failure Modes – MITT Subjects

Earliest Primary Effectiveness Failure Modes	Pulsed Field Group N = 305 Incidence, %1 (Subjects with event)	Difference 95% BCI[1]	Thermal Group N = 302 Incidence, %[1] (Subjects with event)
Any Primary Effectiveness Failure Mode[2]	**26.7 (80)**	**-2.0 [-9.2, 5.2]**	**28.7 (85)**
Acute Procedural Failure	0.8 (2)	-0.0 [-1.5, 1.5]	0.8 (2)

Earliest Primary Effectiveness Failure Modes	Pulsed Field Group N = 305 Incidence, %1 (Subjects with event)	Difference 95% BCI[1]	Thermal Group N = 302 Incidence, %[1] (Subjects with event)
Post-blanking Detectable AF/AFL/AT	17.2 (51)	0.7 [-5.2, 6.7]	16.4 (48)
Post-blanking Detectable AF	11.2 (33)	1.2 [-3.7, 6.1]	10.0 (29)
Post-blanking Detectable AFL	4.8 (14)	-0.4 [-4.0, 3.1]	5.3 (15)
Post-blanking Detectable AT	1.5 (4)	-0.0 [-2.1, 2.0]	1.5 (4)
Post-blanking cardioversion for AF/AFL/AT	0.5 (1)	0.3 [-0.6, 1.5]	0.2 (0)
Post-blanking use of Type I/III AAD	8.1 (24)	-1.1 [-5.6, 3.4]	9.2 (27)
Re-ablation for AF/AFL/AT	0.5 (1)	-0.0 [-1.2, 1.2]	0.5 (1)
Any non-procedural use of amiodarone	0.5 (1)	-2.0 [-4.2, -0.2]	2.5 (7)

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note 1: Point estimate for incidence and incidence difference calculated as the mean of the relevant posterior distribution; posterior mean and Bayesian credible interval calculated Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors and multiple imputation for incomplete data.

Note 2: Each subject has only one earliest primary effectiveness failure mode.

Acute Procedural Success

Acute Procedural Success was defined as demonstration of Acute Vein Success in all attempted PVs using the randomized treatment catheter during the Index/Rescheduled Index Procedure, as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion was made, with or without adenosine.

The proportion of Pulsed Field MITT subjects with Acute Procedural Success was 99.3%, and the proportion of Thermal MITT subjects with Acute Procedural Success was 99.3%. There was not a statistical difference between these results [95% BCI -1.5, 1.5]. There were two acute procedural failures in the Pulsed Field group and two in the Thermal group.

Study Conclusion

The ADVENT Trial results constitute valid scientific evidence that gives reasonable assurance of the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System when used in the treatment of patients with drug-resistant, recurrent, symptomatic paroxysmal atrial fibrillation.

Supplemental Clinical Information: FARA-Freedom Post-Market Clinical Follow-Up Study

Study Title	A Prospective Open-Label Single Arm Post Market Clinical Follow-Up Trial of the FARAPULSE Pulsed Field Ablation System in Patients with Paroxysmal Atrial Fibrillation
Number of Centers	14 sites in Europe
Number of Subjects	180 subjects treated with the FARAPULSE Pulsed Field Ablation System

Objective

The primary objective of the FARA-Freedom Study was to provide ongoing post-market demonstration of the safety and performance of the FARAPULSE Pulsed Field Ablation System in the treatment of patients with Paroxysmal Atrial Fibrillation (PAF), when used commercially in Europe.

Design, Scope and Methods

The FARA-Freedom Study was a prospective, open label, post market study conducted at 14 centers in Europe. All treated subjects were followed for 360 days post-ablation with weekly event monitoring beginning on Day 90, and

72-hour Holter monitoring at Days 180 and 360. Clinical follow-up at Days 7, 30, 90, 180 and 360 were performed to determine any occurrence of adverse events or arrhythmia recurrence. The interim study analysis results from this study were provided as supplementary clinical evidence to support the safety and effectiveness of the FARAPULSE PFA System using statistical analyses that are identical or analogous to the methods used for the ADVENT Trial.

Endpoints

The primary safety endpoint was a Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device or procedure-related SAEs as adjudicated by the CEC.

Acute Primary safety endpoints were the following with an onset date within 7 days of the Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation
- Pericarditis
- Pulmonary edema
- Vascular access complications
- Heart block
- Gastric motility/pyloric spasm disorders

Late onset primary safety endpoints were the following with an onset date any time through the completion of 12-month follow-up visit:

- Pulmonary Vein Stenosis (PVS)
- Atrio-esophageal fistula

The safety hypotheses are as follows:

$H_0: Q_T \geq PG_{saf}$

$H_A: Q_T < PG_{saf}$,

where QT is the probability of an MITT subject experiencing one or more CSE, and PGsaf is a performance goal of 0.14. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the upper bound of a 95% central Bayesian credible interval (BCI) being less than PGsaf. The parameter QT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of QT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis, using the same approach that is used in the ADVENT Statistical Analysis Plan.

The primary performance endpoint was Treatment Success in MITT subjects through the Month 12 Assessment defined as:

1. Acute Procedural Success AND
2. Chronic Success, defined as freedom from:
    a. At the Index / Rescheduled Index Procedure: Use of a non-PFA treatment modality for PVI
    b. After the Blanking Period, occurrence of any Detectable AF, AFL or AT excluding CTI-dependent AFL confirmed by EP study, any cardioversion for AF, AFL or AT (excluding for CTI-dependent AFL), Use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT
    c. At any time re-ablation for AF, AFL or AT (other than for CTI-dependent AFL) or use of amiodarone, except intra-procedurally to control an arrhythmia.

The performance hypotheses are as follows:

$H_0: P_T \leq PG_{perf}$

$H_A: P_T > PG_{perf}$,

where PT is the probability of a subject being a Treatment Success at 12 Months, and PGperf is a pre-specified performance goal of 0.50. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the lower bound of a 95% central Bayesian credible interval (BCI) being greater than PGperf. PT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of PT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis.

Subject Accountability

All subjects who signed and dated the Informed Consent Form were considered enrolled in the study.

Intent-to-Treat (ITT) Subjects are subjects who met all the following criteria:

- The subject signed the informed consent document
- The subject was determined by the site to meet all pre-procedural study eligibility criteria
- The subject began the Index Procedure

Modified Intent-to-Treat (MITT) Subjects are ITT Subjects who received any energy delivery for PVI with the FARAPULSE Pulsed Field Ablation System at an Index / Rescheduled Index Procedure.

A total of 185 subjects were enrolled in the study and a total of 180 subjects were treated with the FARAPULSE Pulsed Field Ablation System. The ITT, MITT, and Safety analysis sets consist of the same population (N=180), as all subjects received energy delivery for PVI with the FARAPULSE Pulsed Field Ablation System.

Study Population Demographics, Baseline Characteristics, and Visit Compliance

The demographics of the study population represented a typical PAF catheter ablation patient. Mean age was 62.3 years and 61.1% were male. Mean LVEF was 60.8 % and mean LAD was 4.0 cm. The mean CHA2DS2-VASc Score was 1.8. Palpitations were the most prevalent baseline AF symptom reported in subjects (76.7%) with a mean frequency of 11.0 palpitations over the previous two-month period. The most common comorbidities were hypertension (55%) and dyslipidemia (38.9%).

Study subjects were scheduled for assessment at Baseline, Index Procedure, Pre-Discharge, Days 7, 30, 60, 90, 180 and Day 360. Visit compliance for these study assessments was high at 99.3% overall, and 96.8% of visits conducted within protocol window. The overall rhythm monitoring weekly compliance was high, with 89.1% of monitored weeks resulting in an evaluable rhythm monitoring record for study subjects .

Procedural Durations

Ablations were performed using the FARAPULSE Pulsed Field Ablation System, with either the 31mm or 35mm FARAWAVE Pulsed Field Ablation Catheter, using a recommended minimum of 8 applications in each PV at between 1.8 and 2.0 kilovolts (kV).

The duration of clinically relevant portions of each Index Procedure were recorded and compared descriptively.

Overall procedure time averaged 72 minutes; this is inclusive of the protocol-required 20-minute wait time following the last ablation. Longer procedure durations occurred in subjects that had an acute reconnection of the PV requiring a touch up to be performed thereby adding an additional 20-minute wait period as specified per protocol. Total ablation time averaged 17.8 minutes. Mean LA dwell time was 40.9 minutes, which is inclusive of the 20-minute wait time post-ablation.

Results

<u>Primary Safety Endpoint</u>

Two (2) subjects experienced one or more CSE events therefore the estimated incidence through 12 months is 1.4%, and the upper bound of the 95% BCI is 3.7%. The posterior probability that the incidence is less than the pre-specified performance goal of 14% is >0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion.

Table 11. Summary of Subjects with one or more CSE

Safety Subjects with One or More CSE Events by Event Type	Number of Subjects % (n / N) N=180
Any CSE Event	1.1 (2/180)
Death	0.0 (0/180)
Myocardial infarction	0.0 (0/180)
Persistent phrenic nerve palsy	0.0 (0/180)
Stroke	0.0 (0/180)
TIA	0.6 (1/180)
Peripheral organ thromboembolism	0.0 (0/180)
Cardiac tamponade or perforation	0.6 (1/180)
Pericarditis	0.0 (0/180)
Pulmonary edema	0.0 (0/180)
Vascular access complication	0.0 (0/180)
Heart block	0.0 (0/180)
Gastric motility/pyloric spasm	0.0 (0/180)
Pulmonary vein stenosis	0.0 (0/180)
Atrio-esophageal fistula	0.0 (0/180)

Note 1: n = number of subjects with event, N = number of safety subjects.

Abbreviations: CSE = Composite Safety Endpoint, TIA = transient ischemic attack

Additional Safety Information

Overall, 137 adverse events were experienced in 69 subjects. There were no incidences of persistent phrenic nerve palsy, no occurrences of pulmonary vein stenosis, and no atrio-esophageal fistulas occurring at any time during study follow-up.

There were no Unanticipated Adverse Device Effects (UADEs) in the FARA-Freedom Study.

Table 12. Summary of Adverse Events

Adverse Events Categories- MITT	All Subjects (N=180) n (%) e[1]
Any adverse event	69 (38%) 137
Any SAE	20 (11%) 31
Any device-related AE	6 (3%) 6
Any procedure-related AE	26 (14%) 31
Any device-related SAE	1 (1%) 1
Any procedure-related SAE	7 (4%) 9

Note 1: N = number of MITT in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Serious Adverse Events

The following table summarizes the incidence of all SAEs by AE Category. There were 7 device- or procedure-related SAEs reported in 9 subjects. One (1) event of TIA was assessed by the CEC as possibly related to the device and probably related to the procedure. All other events were classified as procedure related only by the CEC. All of these SAEs were determined to be resolved by the without reported sequelae.

Table 13. Related Serious Adverse Events by Category – MITT Subjects

Procedure- or Device-Related Serious Adverse Events	All Subjects (N=180) n (%) e[1]
Procedure- or Device-Related Serious Adverse Events	7 (4%) 9
Atrial flutter	1 (1%) 2

Procedure- or Device-Related Serious Adverse Events	All Subjects (N=180) n (%) e[1]
Procedure related Abnormal labs	2 (1%) 2
Angina/Chest Pain - Post EP procedure	1 (1%) 1
Atrial tachycardia/Other SVT	1 (1%) 1
Myocardial Perforation with Tamponade	1 (1%) 1
Pseudoaneurysm	1 (1%) 1
TIA	1 (1%) 1

Note 1: N = number of MITT subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Primary Performance Endpoint

The estimated probability of MITT subjects experiencing Treatment Success was 66.3% (lower bound of the 95% BCI is 59.1, upper bound is 73.1). The posterior probability that this success rate exceeds the pre-specified performance goal of 50% is > 0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion.

Table 14. Primary Performance Endpoint – MITT Subjects

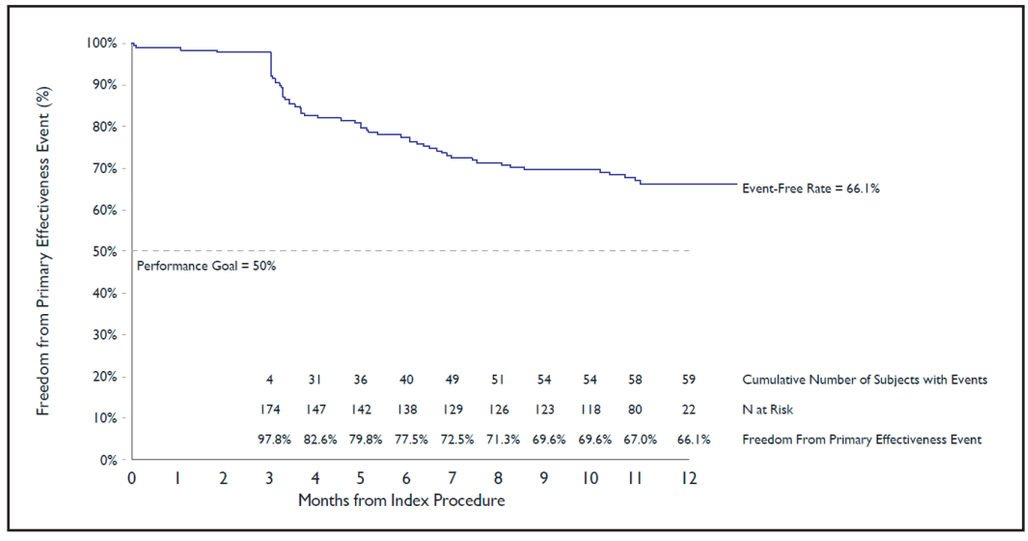
Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] N = 180	Incidence (%)	95% BCI	Posterior Probability of Treatment Success Proportion > 50%
90 [31]	66.3	[59.1, 73.1]	>0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

An additional analysis of the primary performance endpoint was performed using the Kaplan-Meier method to include incomplete subject data. This is a different statistical technique applied to a slightly different definition of the endpoint (time to failure rather than Treatment Success at the 12-month visit), but the Kaplan-Meier estimate of 66.1% at 360 days agrees closely with the 66.3% estimate produced by the pre-specified Bayesian statistical model. These data are displayed in the following graph.

Figure 3. Survival Analysis, Primary Performance Endpoint



The mode of the earliest failure of the primary effectiveness endpoint for each MITT subject is detailed in the following table.

Table 15. Earliest Primary Effectiveness Failure Modes – MITT Subjects

First Primary Effectiveness Failure Mode	Number of Subjects with Event N = 180	Estimated Incidence (%)[1]	95% BCI[1]
Any Primary Effectiveness Failure Mode[2]	59	33.7	[26.9, 40.9]
Acute Procedural failure	0	0.3	[0.0, 1.4]
PVI performed with non-PFA device	0	0.3	[0.0, 1.4]
Post-blanking Detectable AF/AFL/AT/SVT	41	23.6	[17.6, 30.2]
Post-blanking Detectable AF	31	17.9	[12.6, 23.9]
Post-blanking Detectable AFL	0	0.3	[0.0, 1.6]
Post-blanking Detectable AT	8	4.8	[2.2, 8.4]
Post-blanking Detectable SVT	2	1.5	[0.3, 3.9]
Post-blanking cardioversion for AF/AFL/AT	0	0.3	[0.0, 1.6]
Post-blanking use of Type I/III AAD	12	7.1	[3.8, 11.3]
Any re-ablation for AF/AFL/AT	3	2.0	[0.5, 4.6]
Any non-procedural use of amiodarone	3	2.0	[0.5, 4.5]

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note 1: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

Note 2: Each subject has only one earliest primary effectiveness failure mode.

Additional Performance Information

Acute Procedure Success was defined as the proportion of all attempted PVs isolated using the FARAWAVE Pulsed Field Ablation Catheter during the Index procedure, as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing. All ablated PVs achieved Acute Vein success (100%).

Study Conclusion

The primary safety and performance endpoint analysis from the European FARA-Freedom PMCF Study provides supplemental evidence supporting the safety and performance of the FARAPULSE PFA System in the treatment of patients with PAF.

ADVANTAGE Clinical AF Study Phase 1

Study Title	A Prospective Single Arm Open Label Study of the FARAPULSE Pulsed Field Ablation System in Subjects with Persistent Atrial Fibrillation
Number of Centers	43 sites in the North America and Europe
Number of Subjects	355 enrollments, including 79-roll-in subjects, 16 Consent Ineligible/ Intent, and 260 non-roll-in subjects treated with the FARAPULSE Pulsed Field Ablation System.

Objective

The objective of the ADVANTAGE AF Study was to establish the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System (FARAPULSE PFA System) for the treatment of drug refractory, symptomatic persistent atrial fibrillation (PersAF).

Design, Scope, and Methods

The ADVANTAGE AF Phase 1 Study was a prospective, single arm, open label, multi-center IDE pivotal study conducted at 43 sites in the United States (39), Canada (2), and Europe (2). A total of 355 subjects were enrolled in the study and a total of 339 were treated with the FARAPULSE Pulsed Field Ablation System. All subjects who met eligibility criteria, signed the informed consent, and underwent the Index Procedure were followed post-ablation for twelve (12) months with twice per month event monitoring plus symptom-driven event monitoring beginning on Day 90, a 24 Hour Holter monitor at Day 180 and Day 360 and clinical follow ups at Day 7, Day 30, Day 90, Day 180 and Day 360 to determine any occurrence of adverse events or arrhythmia recurrence.

Endpoints

The primary safety endpoint (PSE) was the proportion of Treatment Subjects and Attempt Subjects with one or more of the following device or procedure-related Composite Serious Adverse Events (CSAEs) following the Index Procedure / Rescheduled Index Procedure or the Re-Ablation Procedure within the Blanking Period, with an Onset Date following the procedure as specified in the table below.

Table 16. CSAEs Following Index Procedure/Rescheduled Index Procedure or Re-Ablation Procedure Within 3-Month Blanking Period

Composite Serious Adverse Events	Onset Date
• Death • Myocardial infarction • Stroke • TIA • Peripheral or organ thromboembolism • Pulmonary edema • Unresolved phrenic nerve palsy/paresis • Vascular access complications • Heart block • Gastric motility/pyloric spasm disorders	Day 0 – Day 7
• Cardiac tamponade/perforation • Pericarditis	Day 0 – Day 30
• PV stenosis • Atrio-esophageal fistula	Day 0 – Day 360 Assessment

The primary effectiveness endpoint (PEE) was the proportion of Treatment Subjects with Treatment Success through the Day 360 Assessment.

Treatment Success was defined as:

1. Persistent AF Acute Procedural Success AND
2. Persistent AF Chronic Success, defined as freedom from the following after the 3-month Blanking Period (excluding documented CTI-dependent atrial flutter):
   - **i. Arrhythmia**: Occurrence of any Detectable AF, AFL or AT
   - **ii. Re-ablation:** Any re-ablation for AF, AFL or AT
   - **iii. Cardioversion:** Any electrical cardioversion for AF, AFL or AT
   - **iv. AAD Use:** Use of a Non-Failed Class I / III AAD or amiodarone

Subject Accountability

All subjects who signed and dated the informed consent were considered enrolled in the study and classified as either Roll-In or Non-Roll-In subjects.

Roll-In Subject - The first subject enrolled by each Investigator at each site was treated with the FARAPULSE Pulsed Ablation System as part of Investigator preparation and was enrolled into the study as a Roll-In Subject.

Non Roll-In Subject - After the Roll-in subject criteria was satisfied for the treating physician, Non Roll-In subjects could be enrolled.

Roll-in and Non Roll-In subjects were further classified as Consent Ineligible, Intent, Attempt, or Treatment.

- **Consent Ineligible** – any subject who signed informed consent but was found ultimately not to meet eligibility criteria
- **Intent** – Intent subjects included the following type of subjects
  - Any subject who signed informed consent, met eligibility criteria, but did not have any study investigational devices inserted into the body
  - Any subject that was enrolled in the study but did not undergo the Index Procedure within 30 days from the Consent Date or a Rescheduled Index Procedure within 45 days of the Index Procedure. These subjects were withdrawn from the study as of the end of the above disqualifying interval.
- **Attempt** – any subject who signed informed consent, met eligibility criteria, and had an investigational

device inserted into the body but did not receive any pulsed field ablation application

- **Treatment** – any subject who signed informed consent, met eligibility criteria, had an investigational device inserted into the body and received at least one pulsed field ablation application

A total of 355 subjects (79 Roll-In, 10 Consent Ineligible, 6 Intent and 260 Non-Roll-In Treatment subjects) were enrolled in the ADVANTAGE AF Study Phase 1 across 43 investigational sites in the United States, Canada, and Europe. There were 79 Roll-In subjects and 260 Non Roll-in subjects that received treatment with the FARAPULSE system. Primary analyses were performed on the 260 Non Roll-In Treatment subjects who will henceforth be referred to as "Treatment subjects".

Study Population Demographics, Baseline Parameters, and Visit Compliance

Key baseline demographics and clinical characteristics of the Treatment subjects are presented in Table 17 and 18 below. The mean age of Treatment subjects in the ADVANTAGE AF Study Phase 1 was 66.2 ± 9.3 years. The majority of the subjects were male (69.2%) and all subjects met the eligibility criteria of having a persistent AF diagnosis. As expected with a persistent AF population, the majority of subjects (185, 71.2%) had previously undergone a cardioversion procedure.

Table 17. Baseline Demographics

Characteristic	Measurement	Subjects (N=260)
Age (years)	n Mean ± SD (Median) Range	260 66.2 ±9.3 (67.5) (35.0 - 87.0)
Sex	Male	180 (69.2%)
	Female	80 (30.8%)
Ethnicity	Not disclosed	45 (17.3%)
	Not Hispanic or Latino	211 (81.2%)
	Hispanic or Latino	4 (1.5%)
Race[1]	Not disclosed	45 (17.3%)
	White	209 (80.4%)
	Black or African American	4 (1.5%)
	Asian	3 (1.2%)

n is number of subjects; SD is standard deviation;
Categorical results are number of subjects (% of total subjects [N] with non-missing values).
[1]Subjects may contribute to more than one category

Table 18. Baseline Characteristics

Characteristic	Measurement	Subjects (N=260)
BMI (kg/m2)	n Mean ± SD (Median) Range	260 30.4 ± 5.3 (29.8) (15.0 - 41.9)
LVEF (%)	n Mean ± SD (Median) Range	259 57.2 ± 6.9 (58.0) (40.0 - 73.0)
LA Diameter (cm)	n Mean ± SD (Median) Range	228 4.3 ± 0.6 (4.3) (2.5 - 5.4)
LA Volume (mL)	n Mean ± SD (Median) Range	32 65.1 ± 24.6 (70.0) (25.0 - 100.0)
Cardiac Procedure History	Prior cardiac ablation	9 (3.5%)
	Coronary Artery Bypass Grafting (CABG)	9 (3.5%)
	Valvular Surgery	0 (0.0%)

Characteristic	Measurement	Subjects (N=260)
Cerebrovascular Disease History	Cerebral Vascular Accident (CVA)/Stroke	14 (5.4%)
	Transient Ischemic Attack (TIA)	6 (2.3%)
Cardiovascular Disease History	Hypertension	165 (63.5%)
	Valvular Heart Disease	20 (7.7%)
	Peripheral Vascular Disease	10 (3.8%)
	Coronary Artery Disease	61 (23.5%)
	Acute Myocardial Infarction (MI)	15 (5.8%)
NYHA Functional Class	No Heart Failure	173 (66.8%)
	Class I	42 (16.2%)
	Class II	44 (17.0%)
	Class III	0 (0.0%)
	Class IV	0 (0.0%)
CHA2DS2-VASc Score	0	31 (11.9%)
	1	47 (18.1%)
	2	59 (22.7%)
	3	64 (24.6%)
	4	43 (16.5%)
	5	12 (4.6%)
	6	4 (1.5%)
Comorbidities	Diabetes	44 (16.9%)
	Dyslipidemia	117 (45.0%)
	Obstructive Sleep Apnea	72 (27.7%)
	COPD	17(6.5%)
	Renal Dysfunction/ Failure	7 (2.7%)
History of Refractory or Non-tolerant AADs	Amiodarone	80 (30.8%)
	Dofetilide	15 (5.8%)
	Dronedarone	31 (11.9%)
	Sotalol	47 (18.1%)
	Flecainide	89 (34.2%)
	Propafenone	15 (5.8%)
Anticoagulants at Baseline	DOAC	257 (98.8%)
	VKA	5 (1.9%)

Characteristic	Measurement	Subjects (N=260)
Cardiac Arrhythmia History	History of Atrial Fibrillation[1]	260 (100.0%)
	Paroxysmal Atrial Fibrillation	82 (31.5%)
	Persistent Atrial Fibrillation	260 (100.0%)
	Long Standing Persistent Atrial Fibrillation	0 (0.0%)
	Years since first AF diagnosis	
	n Median (IQR) Range	260 1 (0 - 4) (0 - 41)
	Atrial Flutter	63 (24.2%)
	CTI dependent flutter	41 (15.8%)
	Atypical flutter	8 (3.1%)
	Unknown	10 (3.8%)
	Other flutter[2]	4 (1.5%)
	Atrioventricular Block/Conduction Disease	32 (12.3%)
	1st degree AV block	32 (12.3%)
	2nd degree AV block	0 (0.0%)
	3rd degree AV block	0 (0.0%)
	Sinus Bradycardia	96 (36.9%)
	Sinus Tachycardia	8 (3.1%)
	Ventricular Tachycardia	4 (1.5%)
	Premature Ventricular Contractions	4 (1.5%)
	Right Bundle Branch Block	3 (1.2%)
	Sinus Node Dysfunction	2 (0.8%)
	Junctional Arrhythmia	1 (0.4%)
	Other Cardiac Arrhythmia[3]	9 (3.5%)
Cardioversion History	None	75 (28.8%)
	n Median (IQR) Range	185 1 (1 - 2) (1 - 6)
Baseline 12-lead ECG Rhythm	Atrial Fibrillation	150 (57.7%)
	Sinus Rhythm	88 (33.8%)
	Sinus Bradycardia	14 (5.4%)
	Atrial Flutter	8 (3.1%)

n is number of subjects; IQR is inter-quartile range;
Categorical results are number of subjects (% of total subjects [N] with non-missing values).
[1]Subjects may contribute to more than one category
[2]Other atrial flutter types included: PV flutter, paroxysmal a-flutter, 1:1 AV conduction at 140 bpm, variable with AV block
[3]Other cardiac arrhythmia history included: lbbb; one run of VT lasting 4 beats; SVT and AT; AT, SVT, and atrial bradycardia; ectopic atrial rhythm; ventricular extrasystole; bidirectional block and a left anterior hemi-block with a RBBB; lbbb; possible ectopic atrial rhythm

Follow-up visit compliance (pre-discharge, Day 7, Day 30, Day 90, Day 180 and Day 360) was high with an overall compliance rate of 99.4%. Post-ablation rhythm monitoring included symptomatic and twice per month event monitor transmissions during the evaluation period, 12-Lead ECGs at Day 90 and Day 360, and 24-Hour Holter monitors at Day 180 and Day 360. The overall rhythm monitoring compliance for event monitor transmission, 12-lead ECG, and 24-hour Holter was 73.2%, 94.6%, and 92.2%, respectively.

Procedural Characteristics

The duration of clinically relevant portions of each Index Procedure were recorded descriptively: procedure time (103.0 ± 34.8 minutes), LA dwell time (58.5 ± 19.9 minutes), PVI ablation time (26.8 ± 15.0 minutes), PWI ablation time (18.4 ± 15.0 minutes), and other ablation time (22.6 ± 18.0 minutes). The total procedure time was inclusive of the 20-minute waiting period required per protocol prior to assessing for PV entrance block and inclusive of all ablations, including ablation to the PVs, PW, CTI, and additional lesion sets. Fluoroscopy time was 19.5 ± 13.1 minutes. An anchoring technique of placing a wire within an adjacent PV while using sheath support to position the FARAWAVE PFA Catheter superiorly to ablate antral/ superiorly during posterior wall ablation was optional and utilized in 71.8% of procedures. Additional procedure characteristics can be found in table 19.

Table 19. Additional Index Procedure Characteristics

Characteristic	Measurement	Index Procedures (N=260)
Method of Anesthesia	General anesthesia	226 (86.9%)
	Conscious sedation/Monitored Anesthesia Care (MAC)	34 (13.1%)
Screening for LA Thrombus Performed	Yes	260 (100.0%)
LA Thrombus Identified	Yes	0 (0.0%)
ACT levels Maintained >300	Yes	256 (98.5%)
Other Ablations Using a Commercially Available RF Catheter	Treatment-emergent left AFL	8 (3.1%)
	Treatment-emergent AT	1 (0.4%)
	CTI-dependent AFL	50 (19.2%)
IV fluids administered (mL)	Yes	260 (100.0%)
Volume of IV fluids administered (mL)[1]	Mean ± SD (Median) Range	932.5 ± 532.8 (850.0) (11.0 - 3700.0)
Contrast dye injected	Yes	10 (3.8%)
Volume of contrast dye injected (mL)	Mean ± SD (Median) Range	25.4 ± 21.3 (23.0) (5.0 - 65.0)
PFA Applications	PVI	45.1 ± 9.3
	PWI	32.0 ± 12.7
Same Day Discharge	Same Day	141 (54.2%)

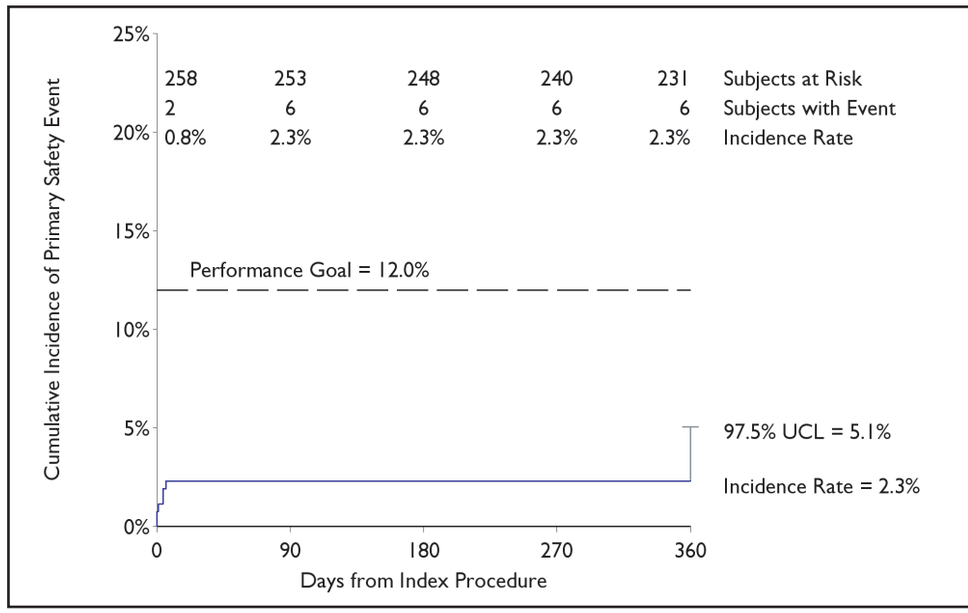
[1]3 procedures with unknown IV fluid volume

Results

Primary Safety Endpoint

Out of 260 Treatment subjects, 6 subjects experienced a device- or procedure-related Composite Serious Adverse Event (CSAE) through Day 360 for a cumulative primary safety event incidence rate of 2.3% (Figure 4). The 97.5% one-sided upper confidence limit (UCL) of the cumulative incidence rate was 5.1%, which was lower than the predefined performance goal of 12%. Therefore, the Primary Safety Endpoint was met.

Figure 4. Primary Safety Endpoint Result



The device- or procedure-related CSAEs that occurred following the Index Procedure are summarized in Table 20. Each event was classified by the ADVANTAGE AF Clinical Events Committee (CEC) following pre-defined CSAE definitions.

Table 20. Primary Safety Events

Primary Safety Event Type	Subjects with an Event[1] (% of Total Subjects) (N=260)
Myocardial Infarction	1 (0.4%)
Pericarditis	1 (0.4%)
Pulmonary edema	4 (1.5%)

[1]Subjects may experience multiple Primary Safety Endpoint event types.

Additional Safety Information

Related Adverse Events

There were a total of 55 serious adverse events reported in 44 (16.9%) Treatment subjects. A total of 26 (47.3%) serious adverse events were adjudicated by the CEC as not device or procedure related. The remaining 29 events were adjudicated as serious and procedure related with a subset of 5 events also adjudicated as device related (Tables 21 and 22). The device related serious adverse events included one (1) oozing/ bleeding event, adjudicated by the CEC as related to the FARADRIVE Steerable Sheath, 3 arrhythmia events, adjudicated as unrelated to the PFA catheter and sheath but related to another component of the FARAPULSE PFA system, and one (1) hemolysis event, further described below.

A total of 29 procedure related serious adverse events occurred in 22 (8.5%) Treatment subjects. The largest category of procedure related serious adverse event was genitourinary/renal with 7 events in 6 Treatment subjects. Details of the 7 serious genitourinary/renal events are as follows: 4 urinary retention events, 2 hematuria events, and one (1) acute kidney injury. This acute kidney injury was attributed to dehydration by the investigator but no hemolysis biomarkers (e.g., haptoglobin and plasma free hemoglobin) were tested. This procedure related serious adverse event resolved with intravenous fluid hydration.

Two Treatment subjects had procedure-related acute kidney injury, resulting in a rate of procedure-related acute kidney injury of 0.8% in the Non Roll-In Treatment subjects. One acute kidney injury was considered to be secondary to dehydration as discussed above. The other acute kidney injury occurred secondary to intravascular hemolysis (laboratory confirmed) and was adjudicated by the CEC as a procedure-related serious adverse event. This subject received 93 total PFA applications and sustained acute kidney injury (with elevation of creatinine from 1.2 to 2.3 mg/dL) before normalizing with conservative management.

There was one (1) acute coronary syndrome requiring percutaneous coronary intervention and stent placement

reported in Treatment subject who suffered an acute myocardial infarction during the index procedure. Coronary angioplasty report noted that the etiology of the acute myocardial infarction was unclear but there was presence of clot and vasospasm in otherwise normal arteries. The adverse event was adjudicated by the CEC as an acute myocardial infarction, a primary safety event, related to the index procedure but unable to determine its relationship to the study catheter, sheath, or any other component of the ablation system.

There was one peripheral embolic event reported in a Treatment subject (0.4%). It was a renal infarction that occurred three (3) weeks post procedure in a subject who received 60 PFA applications during the index procedure. The CEC adjudicated the event as procedure-related serious adverse event, not related to the study catheter or sheath, but unable to determine if it was related to any other component of the ablation system.

Table 21. Procedure-related Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Total	22 (8.5%)	29
Procedure related Genitourinary/Renal	6 (2.3%)	7
Procedure related Anesthesia/Sedation	1 (0.4%)	1
Oozing/Bleeding	2 (0.8%)	2
Atrial Fibrillation (AF)	4 (1.5%)	4
Atrial tachycardia/Other SVT (e.g. AVRT, AVNRT, EAT)	2 (0.8%)	2
Procedure related Heart Failure	3 (1.2%)	3
Procedure related Pulmonary (including cough, hemoptysis)	2 (0.8%)	2
Fluid volume overload	1 (0.4%)	1
Hemolysis (Laboratory confirmed)*	1 (0.4%)	1
Procedure related Hypotension	1 (0.4%)	1
Coronary artery injury/Spasm	1 (0.4%)	1
Genitourinary	1 (0.4%)	1
Multiple Heart Failure symptoms	1 (0.4%)	1
Post procedure infection/sepsis	1 (0.4%)	1
Renal Infarction	1 (0.4%)	1

*Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

Table 22. Device-related* Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Total	5 (1.9%)	5
Atrial tachycardia/Other SVT (e.g. AVRT, AVNRT, EAT)	2 (0.8%)	2
Atrial Fibrillation (AF)	1 (0.4%)	1
Hemolysis (Laboratory confirmed**)	1 (0.4%)	1
Oozing/Bleeding	1 (0.4%)	1

*All device-related events were also classified as procedure-related. Events appear in both Table 21 and 22.

**Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

In addition, there were 75 procedure related non-serious adverse events reported in 50 (19.2%) subjects. These included 10 procedure related genitourinary/ renal events reported in 10 subjects (3.5%), which consisted of one (1) urinary tract infection, 2 hematuria, and 7 urinary retention/ decreased urine output. There was also one (1) non-serious procedure related adverse event reported as laboratory confirmed hemolysis in a subject who presented with choluria; and there was one (1) temporary phrenic nerve injury reported in a Treatment subjects (0.4%), as seen in Table 23.

Table 23. Select Procedure-related Non-Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Non-Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Procedure related Genitourinary/Renal	10 (3.8%)	10
Hemolysis (Laboratory confirmed*)	1 (0.4%)	1
Phrenic nerve injury temporary	1 (0.4%)	1

*Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

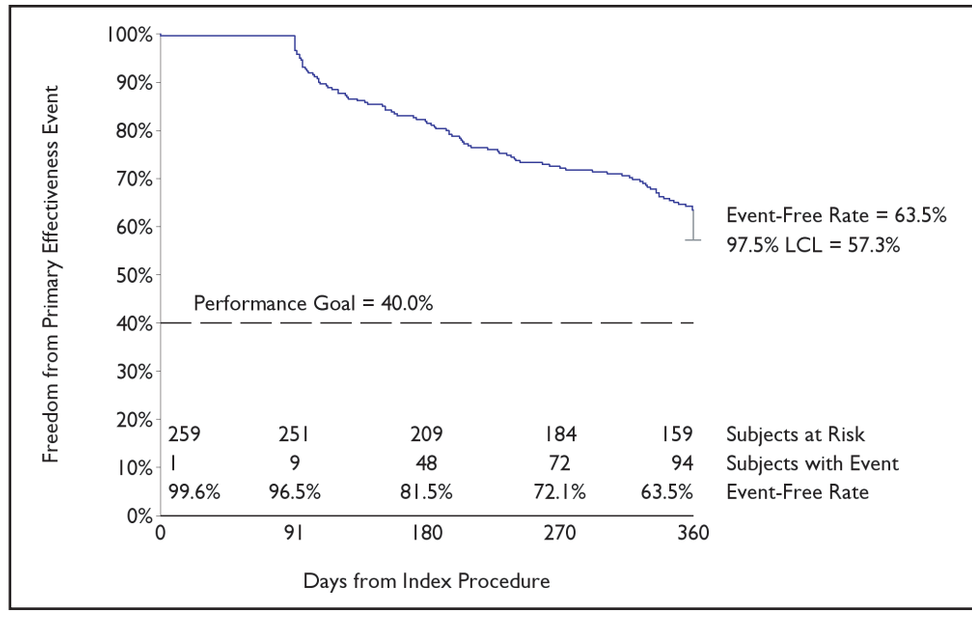
Primary Effectiveness Endpoint

Of the 260 Treatment subjects that underwent an Index Ablation Procedure, 259 (99.6%) reported acute procedural success. One subject was classified as an acute procedural failure due to repeated console errors which required the operator to switch to an RF catheter to complete the procedure. All subjects, including the subject whose procedure was completed using RF, had PVI and PWI achieved.

The second component of the primary effectiveness endpoint is chronic success. Of the 260 Treatment subjects, 93 (35.8%) subjects experienced at least one mode of chronic treatment failure through 360 days of follow-up.

In total, 94 subjects experienced a primary effectiveness failure event through Day 360 post-Index Procedure resulting in a Treatment Success rate of 63.5% with a one-sided 97.5% lower confidence limit (LCL) of 57.3% (Figure 5). Since the LCL was greater than the pre-specified performance goal of 40%, the Primary Effectiveness Endpoint was met.

Figure 5. Freedom from Primary Effectiveness Failure at Day 360



The first and subsequent primary effectiveness failure events are summarized in Table 23. Each subject was considered an endpoint failure at the time of the first event. Subsequent events are presented for completeness. The most common reason for treatment failure was documented AF/AT/AFL post-blanking period and the majority of the documented arrhythmia recurrences was AF.

Table 24. Primary Effectiveness Failure Events

	Subjects with an Event (% of Total Subjects) (N = 260)	
Primary Effectiveness Event Type	**First Failure Event**	**All Failure Events[1]**
Acute procedural failure	1 (0.4%)	1 (0.4%)
Use of a non-study ablation catheter	1 (0.4%)	1 (0.4%)
Documented AF/AT/AFL post-blanking period	79 (30.4%)	88 (33.8%)
≥30 seconds recorded on Event Monitor	65 (25.0%)	76 (29.2%)

	Subjects with an Event (% of Total Subjects) (N = 260)	
Primary Effectiveness Event Type	**First Failure Event**	**All Failure Events[1]**
≥30 seconds recorded on Holter Monitor	8 (3.1%)	33 (12.7%)
≥10 seconds recorded on 12-Lead ECG	6 (2.3%)	26 (10.0%)
AAD use post-blanking period	11 (4.2%)	19 (7.3%)
Use of a non-failed Class I/III AAD post-blanking period	7 (2.7%)	12 (4.6%)
Amiodarone use post-blanking period	4 (1.5%)	7 (2.7%)
Cardioversion for AF/AT/AFL post-blanking period	2 (0.8%)	17 (6.5%)
Re-ablation for AF/AT/AFL post-blanking period	1 (0.4%)	12 (4.6%)

N is total Treatment subjects
[1]Subjects may have multiple failure event types.

Additional Effectiveness Analyses

1. Single Procedure Treatment Success

Single Procedure Treatment Success was defined as freedom from Primary Effectiveness Endpoint failure without a re-ablation procedure for AF, AFL, or AT. There were two Treatment subjects who had re-ablations using the FARAWAVE Catheter during the blanking period and therefore contributed additional failures for the Single Procedure Treatment Success endpoint. However, both subjects experienced atrial arrhythmia recurrence following the blanking period and were therefore already considered effectiveness failures in the Primary Effectiveness Endpoint. Thus, the proportion of subjects with Single Procedure Treatment Success was identical to the proportion of subjects with Primary Effectiveness Endpoint success, 63.8% (166/260) in the Non Roll-In Treatment subjects.

2. Off Drug Treatment Success

Off Drug Treatment Success was defined as freedom from Primary Effectiveness Endpoint failure without the use of a Class I or III AAD after the blanking period, including the use of a failed dose. The Off Drug Treatment Success rate was 56.9% (148/260) in the Non Roll-In Treatment subjects.

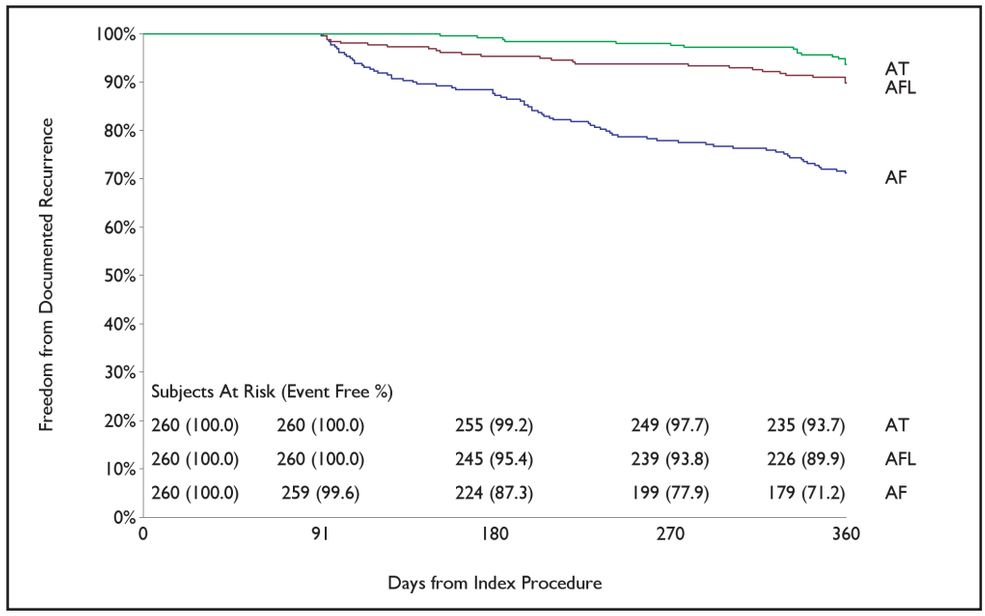
3. Re-Ablation Rate

The Re-Ablation Rate was defined as the proportion of subjects who received one or more re- ablation for AF, AFL, or AT during study follow-up. Among the 260 Non Roll-In Treatment subjects, 14 subjects (5.4%) had one or more repeat ablations during follow-up (two had repeat ablation during the blanking period and 14 had repeat ablation following the blanking period).

4. Type of Recurrence

Of the 260 Treatment subjects, 88 (33.8%) had documented AF, AFL, or AT recurrence post-blanking period (Table 21). There were 51 subjects (19.6%) with only AF recurrence, 5 subjects (1.9%) with only AFL recurrence, and 7 subjects (2.7%) with only AT recurrence. The remaining 25 subjects experienced more than one type of atrial arrhythmia recurrence. The rate of freedom from documented recurrence of each arrhythmia type through Day 360 was 71.2% for AF, 89.9% for AFL, and 93.7% for AT (Figure 6).

Figure 6. Freedom from Documented Recurrence by Rhythm

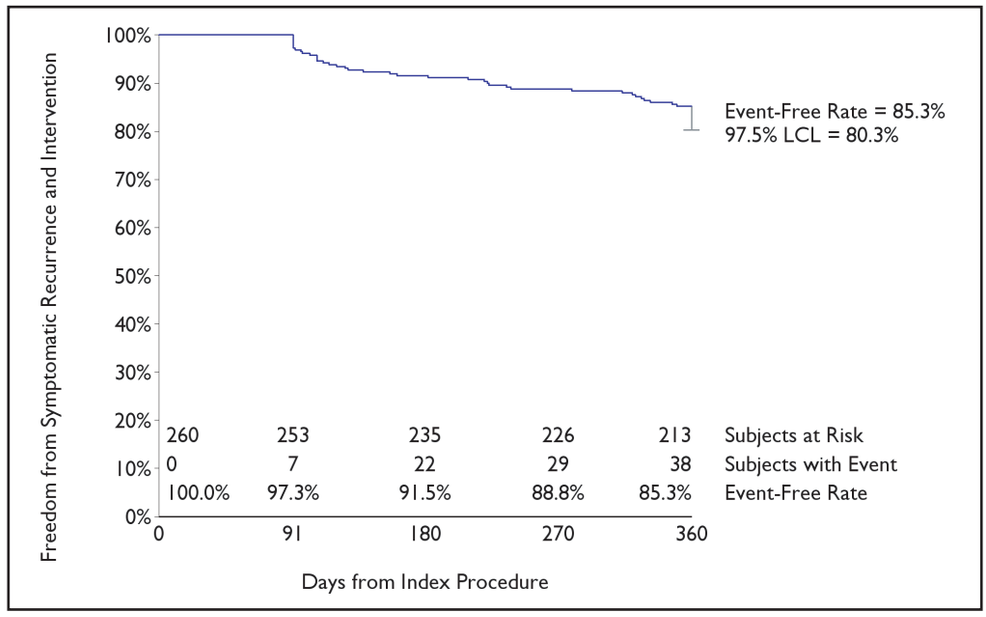


5. Freedom from Documented Symptomatic Recurrence

Given the low rates of re-ablation, AAD use, and cardioversions observed for the Primary Effectiveness Endpoint, a post-hoc analysis was performed to assess the impact of failures due to asymptomatic recurrence only. Subjects who experienced asymptomatic AF, AT, or AFL recurrence meeting the Primary Effectiveness Endpoint definition but had no intervention to treat the recurrence (re-ablation, cardioversion, or prescription of a non-failed Class I/III AAD or amiodarone) and had no reported symptomatic recurrence recorded by event monitor, were considered to have Treatment Success, rather than Treatment Failure in the post-hoc analysis.

The rate of subjects with freedom from symptomatic recurrence or intervention to treat recurrence was 85.3% (Figure 7).

Figure 7. Freedom from Documented Symptomatic Recurrence



Quality of Life Assessments

Subjects were asked to complete Quality of Life (QOL) questionnaires at the Baseline visit, Day 180, and Day 360 Assessments. The EQ-5D-5L was used to measure subjects' health-related quality of life and the Atrial Fibrillation Effect on Quality of Life (AFEQT) was used to evaluate AF specific quality of life.

All questionnaire scores, including sub-component scores, improved by the Day 180 Assessment with the overall AFEQT score increasing by a median of 24 (IQR:10-47) points and EQ-5D-5L score increasing by 5 (IQR:0-15) points.

The improved scores were maintained through the Day 360 Assessment.

Study Conclusions

The ADVANTAGE AF Phase 1 Trial results demonstrated the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System for PV isolation and left atrial posterior wall isolation to treat patients with drug refractory symptomatic persistent atrial fibrillation (episode duration less than one year).

HOW SUPPLIED

Device Details

One (1) FARAWAVE Catheter is supplied sterile using an Ethylene Oxide (EO) process.

WARNING: Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury.

Handling and Storage

Handling	Storage
	Store in a cool, dry, dark place.

Handling excursions between -29 °C and 60 °C degrees permitted. Do not use if the FARAWAVE Catheter is exposed to environmental conditions beyond this range.

OPERATIONAL INSTRUCTIONS

Compatible Related Devices

Intracardiac electrophysiology and cardiac ablation procedures should be performed in a fully equipped clinical electrophysiology lab. In addition to the FARAWAVE Catheter, the following devices and materials are intended to be used:

- FARADRIVE Sheath
- Compatible BSC Generator
- Compatible BSC Recording System Module
- Compatible FARASTAR Catheter Connection Cable
- Standard commercially available 0.035 in (0.89 mm) guidewires

Preparation

WARNING: Before use, inspect the packaging for any violation of the sterile barrier and inspect the FARAWAVE Catheter for any defects. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire. Do not use potentially contaminated or defective equipment.

WARNING: Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.

Please refer to the operator's manuals and Instructions for Use for the compatible BSC Generator, FARASTAR Catheter Connection Cable and the FARADRIVE Sheath for instructions on connecting and operating these systems in conjunction with the FARAWAVE Catheter. Use appropriate accessory cables to connect the catheter to the appropriate accessory equipment.

1. Connect the patient to an ECG recording system to facilitate arrhythmia monitoring per the standard operating procedure of the electrophysiology lab or manufacturer's operator's manual.

   Note: This should be done prior to introducing any intracardiac catheters.

   ---

2. Open the FARAWAVE Catheter package. Carefully transfer the package contents into the sterile field, maintaining aseptic technique.
3. Connect the FARAWAVE Catheter to a compatible BSC PFA Generator using a FARASTAR Catheter Connection Cable, maintaining aseptic technique. Ensure that the cable/catheter connection remains dry throughout the procedure. For connection information, refer to the FARASTAR Catheter Connection Cable IFU for additional connection instructions.

Note: If a three-dimensional (3-D) catheter navigation and mapping system is going to be used, please follow the standard operating procedure of the electrophysiology lab or the instructions for use contained in the manufacturer's operator's manual.

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4. Turn on the PFA Generator.
5. Obtain femoral vein access under aseptic conditions. Then place an introducer sheath into the vein using a standard percutaneous technique.
6. Obtain left atrial, transseptal access using standard techniques and commercially available equipment. (Refer to the FARADRIVE Sheath IFU for guidance on transseptal access and placement of the FARADRIVE Sheath.)
7. Flush the guidewire lumen and flush port lumen with sterile saline. Connect the flush port to a continuous flush line with pressurized heparinized saline and purge the catheter and tubing of all air bubbles. Ensure all luer fittings are secure.

WARNING: Always verify that the tubing set, catheter, sheath and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing, catheter or sheath can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system.

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8. Insert a standard commercially available 0.035" guidewire through the FARAWAVE Catheter until the tip of the wire is aligned with the tip of the catheter.

Caution: Device deployment friction is increased when attempting to deploy the device when the catheter shaft is bent. FARAWAVE Catheter deployment should always occur with the catheter shaft as straight as possible.

Procedure

Standard procedures for electrophysiology studies will be followed.

WARNING: Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboembolism if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post procedure according to the institution's standards to minimize bleeding and thrombotic complications.

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1. Before placing the FARAWAVE Catheter in the sheath, begin continuous irrigation.

WARNING: Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism.

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2. Compress the splines of the FARAWAVE Catheter for insertion and allow flush to fill the compressed spline array prior to inserting the sheath.

WARNING: Use both fluoroscopy, or other visualization techniques such as echocardiography, and intracardiac electrograms to monitor the advancement of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade.

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3. Advance the FARAWAVE Catheter and the guidewire together into the FARADRIVE Sheath taking care to avoid introducing air into the sheath.
4. Once the distal end of the FARAWAVE Catheter has been fully inserted through the valve, slowly aspirate and flush the FARADRIVE Sheath. Refer to the FARADRIVE Sheath IFU for additional instructions on minimizing air ingress.
5. Under standard imaging guidance (e.g. fluoroscopy or echocardiography), track the guidewire to the target pulmonary vein.
6. Advance the FARAWAVE Catheter over the guidewire into the left atrium. Ensure the tip of the catheter is not bent as it advances beyond the sheath. Ensure the proximal marker band on the catheter is within or beyond the marker band at the tip of the sheath.

CAUTION: Avoid allowing the distal end of the catheter to be put into an acute bend, particularly when advancing the catheter beyond the sheath or deploying the catheter. A catheter exchange may be necessary if the catheter deploys improperly.

7. Check that the distal portion of the FARAWAVE Catheter is free to move. Under standard imaging guidance, carefully deploy the distal splines by pressing down the button and sliding it proximally until the splines deploy into the desired shape. Deployment locks when the button is released.

WARNING: Do not deploy the catheter with any portion of the distal splines located within the sheath as it could lead to catheter damage which may result in patient harm.

WARNING: Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.

8. Position the FARAWAVE Catheter at the ostium of the targeted pulmonary vein. Use both standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the catheter splines and electrodes while obtaining good tissue apposition. Ensure a stable position is achieved before delivering PFA.
9. If applicable, apply sedative bolus per site protocol.
10. Follow the recommended ablation parameters in the table below. (Refer to the PFA Generator IFU for detailed instructions.)

Note: The following table details nominal dose parameters for PV isolation with PFA.

Parameter	Nominal Value (Per PV)
Voltage Amplitude	1.8 kV, 1.9 kV or 2.0 kV
Total PFA Applications	8
PFA Applications in Full Deployment	4
PFA Applications in Partial Deployment	4

Note: Some anatomies may restrict the ability to achieve the partial or full deployment state. In these cases, ablations may be performed in the achievable full or partial deployment state. Incomplete or interrupted deliveries should be repeated.

Note: If spline inversion occurs during manipulation, undeploy the catheter within the body of the left atrium and retract the catheter into the sheath. Rotate the catheter handle 180 degrees while contained within the sheath tip, then insert the cage back into the chamber and attempt deployment again without contacting any

anatomical surfaces. If unsuccessful then remove catheter from the patient to inspect the cage and replace it if needed.

11. Deliver ablation from the PFA Generator at the selected output setting.
12. When ablation is complete, verify that the position of the FARAWAVE Catheter has not changed.
13. Deliver an additional application in the same location. Total number of applications at this site is now two (2).
14. Rotate the FARAWAVE Catheter and reposition at the PV ostium using standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the splines and electrodes while obtaining good tissue apposition. The splines should engage the vein in a different position than the previous two ablations. Ensure a stable position is achieved before delivering PFA.
15. Deliver an additional set of two (2) applications. Total number of applications at this site is now four (4).
16. Retract the FARAWAVE Catheter over the guidewire. Change the deployment shape and re-advance to the target ablation site. The splines should engage the vein in a different position than the previous two positions. Ensure a stable position is achieved before delivering PFA.
17. Deliver an additional set of two (2) applications. Total number of applications at this site is now six (6).
18. Rotate the FARAWAVE Catheter and reposition at the PV ostium using standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the splines and electrodes while obtaining good tissue apposition. The splines should engage the vein in a different position than the previous two ablations. Ensure a stable position is achieved before delivering PFA.
19. Deliver an additional set of two (2) applications. Total number of applications at this site is now eight (8).
20. If needed, perform additional ablations.

Note: After energy delivery, the PFA Generator automatically routes the FARAWAVE Catheter electrodes to the EGM Connector. Signals formed from these electrodes can be viewed on the Recording/Mapping System.

Caution: Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed in the table above, regardless of absence of intracardiac signal.

Catheter Deployment for the Left Atrial Posterior Wall (LAPW) Isolation

1. Check that the distal portion of the FARAWAVE Catheter is free to move. Under standard imaging guidance, carefully deploy the distal splines by pressing down the slider and moving it down the handle until the splines form into the fully deployed configuration. Lock the deployment by releasing the slider. Refer to Figure 1 for a depiction of full catheter deployment.
2. Retract the FARAWAVE Catheter over the guidewire until the splines contact the mouth of the sheath or shaft electrode is at the mouth of the sheath.
3. Retract the guidewire until it is completely inside the FARAWAVE Catheter's guidewire lumen.

WARNING: When positioning on cardiac structures, the guidewire should be retracted to prevent cardiac perforation or tissue damage.

4. Advance and/or rotate the FARAWAVE Catheter and the FARADRIVE Sheath together to position it at the desired location on the LAPW. Adjust the positioning of the catheter and sheath as needed to ensure uniform deployment of the catheter splines and electrodes while at the same time obtaining good tissue apposition.
5. Verify the catheter position using standard imaging guidance. Views from other imaging modalities, including electroanatomical mapping system may be used to supplement fluoroscopy.
6. If applicable, apply sedative bolus per site protocol.
7. Deliver ablation from the PFA Generator using a 1.8 kV, 1.9 kV or 2.0 kV setting.

8. When the application is complete, verify that the position of the FARAWAVE Catheter has not changed.
9. Repeat step 7 for a minimum of two applications per catheter site on the LAPW.
10. After completion of the final application at a site, reposition the catheter to the next site on the LAPW, overlapping it with the previous position one-half of the diameter of the fully deployed configuration footprint, and the repeat steps 4 through 9.
11. Continue ablation across the left atrial posterior wall until posterior wall isolation is complete.

Note: After energy delivery, the PFA Generator automatically routes the FARAWAVE Catheter electrodes to the EGM Connector. Signals formed from these electrodes can be viewed on the Recording/Mapping System.

Caution: Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed above, regardless of absence of intracardiac signal.

Note: An optional anchoring technique was used to perform PW ablation in 71.8% of procedures in the ADVANTAGE AF Phase 1 clinical study. To perform this technique, place the wire in the adjacent PV to anchor the guidewire. Then use the sheath to position the catheter to the location of intended antral ablation.

End of Procedure

1. Under standard imaging guidance (e.g. fluoroscopy or echocardiography), track the guidewire to any pulmonary vein.
2. Carefully un-deploy the FARAWAVE Catheter and retract the catheter over the guidewire until it is completely inside the FARADRIVE Sheath.

WARNING: The FARAWAVE Catheter tip and guidewire move forward during device undeployment. Device deployment and undeployment should be visualized using fluoroscopy. Failure to do so may result in catheter damage and/or patient injury.

3. Retract the guidewire into the FARADRIVE Sheath.
4. Carefully withdraw the FARAWAVE Catheter, along with the guidewire, from the body through the FARADRIVE Sheath using caution to avoid introducing air into the sheath upon removal.
5. Carefully withdraw the FARADRIVE Sheath from the left atrium in accordance with its IFU.
6. Turn off the PFA Generator.

Disposal

To minimize risk of infection or microbial hazards after use, dispose of device and packaging as follows:

After use, the catheter may contain biohazardous substances. The catheter and packaging should be treated and disposed of as biohazardous waste in accordance with any applicable hospital, administrative, and/or local government regulations. Use of a biohazardous container with biological hazard symbol is recommended. Untreated biohazardous waste should not be disposed of in the municipal waste system.

Post-Procedure

Carefully monitor patient while in recovery to ensure hemostasis is achieved and any complications are immediately treated.

Complaint Reporting

In the event that a serious incident occurred in relation to the device, including all patient deaths for procedures where the FARAPULSE product was used, the event should be reported to Boston Scientific and the appropriate regulatory agency.

Boston Scientific's local contact information may be found at: www.bostonscientific.com

Return any catheter related to a complaint, patient harm, injury, or death to Boston Scientific using a BSC Returned Product Kit.

- Returning products for analysis and providing product performance observations helps drive higher reliability on an ongoing basis.
- Be sure to follow the instructions with regard to packaging and shipping any biohazard devices taking care not to expose the handle or connector to fluid that may compromise the catheter and limit analysis.

PATIENT COUNSELING INFORMATION

The physician should consider the following points while counseling patients on the use of the FARAWAVE Catheter in association with the electrophysiological cardiac interventional procedure:

- Discuss the risks and benefits including review of potential adverse events listed in this document.
- Discuss post procedure instructions, including any lifestyle changes, medications, when to call the Healthcare Provider (HCP) and any post procedure follow-up that might be needed.

WARRANTY

For device warranty information, visit www.bostonscientific.com/warranty.

SYMBOL DEFINITIONS

Commonly used medical device symbols that appear on the labeling are defined at www.bostonscientific.com/SymbolsGlossary.

Additional symbols are defined at the end of this document.

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), EIFU, FARAWAVE 1.0 PERSAF, en, 51967689-01A

Contents

Maximum Guidewire OD

Boston Scientific Corporation
300 Boston Scientific Way
Marlborough, MA 01752 USA
USA Customer Service +1-888-272-1001

www.bostonscientific.com

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< en >

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), EIFU, FARAWAVE 1.0 PERSAF, en, 51967689-01A

Black (K) ΔE ≤5.0 / CMYK

FARAWAVE™
FARAWAVE™ NAV

Pulsed Field Ablation Catheters

REF M004PF41M431; M004PF41M432;
M004PF41M411; M004PF41M412

℞ ONLY

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

TABLE OF CONTENTS

REUSE WARNING

Contents supplied STERILE using an ethylene oxide (EO) process. Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific (BSC) representative.

For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

Carefully read all ancillary device instructions prior to use. Observe all contraindications, warnings and precautions noted in these instructions. Failure to do so may result in patient complications.

DEVICE DESCRIPTION

The FARAWAVE Pulsed Field Ablation (PFA) Catheter (henceforth referred to as the FARAWAVE Catheter) is a component of the FARAPULSE PFA System. The FARAWAVE Catheter is a 12F catheter and is compatible with the FARADRIVE Steerable Sheath (henceforth referred to as the FARADRIVE Sheath).

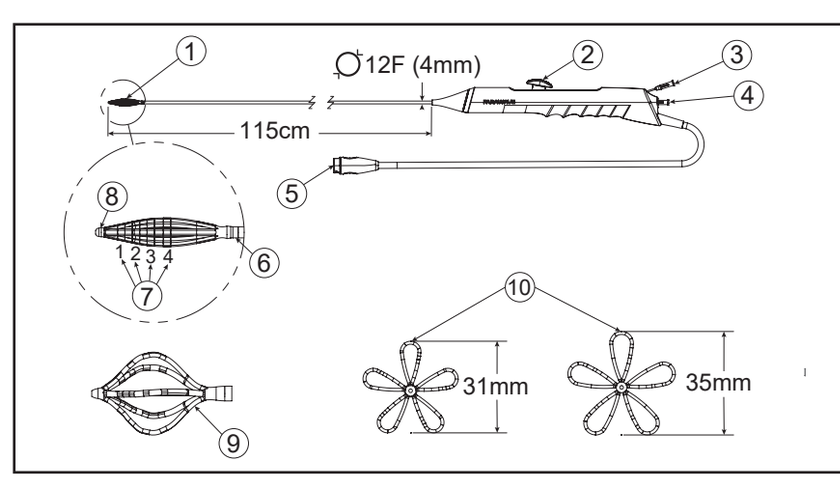


Figure 1.FARAWAVE Catheter
(1) Distal splines (2) Deployment mechanism (3) Flush port (4) Guidewire hub (5) Cable connector (6) Radiopaque marker (7) Four electrodes on five splines (8) Radiopaque tip (9) Partial ("basket") deployment (10) Full ("flower") deployment

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324H) eIFU, MB, FARAWAVE 2.0 PERSAF, US, en, 51967690-01A

The FARAWAVE Catheter is available in two sizes, 31 mm and 35 mm, representative of the fully deployed diameter. Both sizes of the FARAWAVE Catheter are available in both NAV and non-NAV enabled versions.

FARAWAVE NAV incorporates a position sensor for magnetic tracking, navigation, and pose and orientation visualization when used with a compatible BSC Mapping System and FARAVIEW software. Henceforth, both NAV and non-NAV versions of the FARAWAVE catheter will be generically referred to jointly as FARAWAVE Catheter, unless otherwise noted.

The FARAWAVE Catheter is an over-the-wire, multi-electrode catheter designed to deliver PFA energy to the distal section for cardiac ablation. The FARAWAVE Catheter distal section consists of five splines with four electrodes located on each spline, twenty electrodes total.

The FARAWAVE Catheter handle features a deployment mechanism that enables the ability to deploy the distal section into multiple configurations, where the partially deployed configuration is a "basket" shape and the fully deployed configuration is a "flower" shape.

The symbols on the FARAWAVE Catheter handle indicate each configuration:

Table 1. FARAWAVE Catheter Configurations

Symbol	Configuration
	Undeployed
	Partially deployed ("basket")
	Fully deployed ("flower")

For ablation, the FARAWAVE Catheter is designed to be used with the FARASTAR Catheter Connection Cable and FARASTAR Generator.

Contents

One (1) sterile FARAWAVE Catheter

Materials

Contains Cobalt; CAS No 7440-48-4; EC No. 231-158-0. Defined as a 1B according to the European Commission in a concentration above 0.1% weight by weight.

Note: This device is made with a metal alloy which contains cobalt. Current scientific evidence supports that metal alloys containing cobalt used in medical devices do not cause an increased risk of cancer or adverse reproductive effects.

Non-pyrogenic

This device meets pyrogen limit specifications for all patient-contacting parts.

INTENDED USE/INDICATIONS FOR USE

The FARAWAVE Catheter is indicated for:

- the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).
- the isolation of pulmonary veins and the posterior wall in the treatment of drug-refractory, symptomatic Persistent Atrial Fibrillation (episode duration less than one year).

Intended Patient Population

The FARAPULSE PFA System is intended for adult cardiac arrhythmia patients who are age 18 or older.

CONTRAINDICATIONS

The FARAWAVE Catheter is contraindicated for use:

- in patients with active systemic infection;

- in patients with a mechanical prosthetic heart valve through which the catheter must pass;
- in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation;
- in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation;
- in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach;
- in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels);
- via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch.

WARNINGS

- If the visibility of the EP catheter is compromised for any reason, the user should stop and not resume ablation therapy until catheter visibility is established in order to prevent patient injuries such as perforation, heart block and injury to adjacent structures.
- Cardiac mapping and ablation procedures should be performed only by physicians thoroughly trained in invasive cardiology, in the techniques of mapping and ablation, and in the specific approach to be used, in a fully equipped electrophysiology lab. Device specific physician in-service training is made available by the manufacturer.
- Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboembolism if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post procedure according to the institution's standards to minimize bleeding and thromboembolic complications.
- Carefully read all equipment and ancillary device instructions required for the procedure prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient complications.
- Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury.
- Before using, inspect the FARAWAVE Catheter for any defects or physical damage, including electrical insulation on the cables and the catheter shaft that, if used, may cause patient and/or user injury. Do not use defective or damaged devices. Replace damaged equipment if necessary. No modification of this equipment is allowed.
- Electromagnetic Interference (EMI) from any source during normal operation may adversely affect the visualization and tracking of the catheter during the procedure, which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Please reference the FARASTAR capital equipment IFU for instructions for maintaining basic safety and essential performance with regard to electromagnetic disturbances.
- Use of the FARAWAVE Catheter with generators other than a compatible BSC PFA Generator can lead to unexpected energy delivery resulting in either insufficient ablation treatment or over-delivery of energy leading to possible patient hazardous events such as thrombus formation, tissue damage, etc.
- Patients undergoing ablation are at risk for complete AV block which requires the implantation of a temporary and/or permanent pacemaker.
- When the catheter is in the patient, the patient and/or the catheter connector should not come in contact with grounded metal surfaces to minimize the potential for electrical shock.
- Ensure that the cable/catheter connection remains dry throughout the procedure in order to prevent electric shock or other patient injuries as well as to prevent loss of device function.

- Fibrin may accumulate in or on the sheath/catheter assembly during the procedure. Aspirate when removing the catheter.
- In the presence of anticoagulation, there may be an increased risk of bleeding from all causes.
- Electrical recording or stimulation equipment must be isolated. Current leakage from any electrical equipment that is connected to the patient must not exceed 10 microamps for intracardiac electrodes.
- Care must be taken to ensure that any equipment used in connection with the FARAWAVE Catheter be type CF, be defibrillation proof, meet IEC 60601-1 electrical safety requirements, and comply with all local regulatory requirements for specified intended use to reduce the potential risk of inadvertent electrical shock.
- Do not directly touch the patient or any conductive surface when ablation energy is being delivered to prevent the risk of electric shock. Contact with patient or a conductive surface during energy delivery could result in discomfort.
- Stimulation of cardiac tissues caused by pacing stimulus and/or ablation energy may lead to inadvertent induction of arrhythmias. These arrhythmias may require defibrillation that could also result in skin burns.
- Warnings for patients with implantable pacemakers (PPMs) and Implantable Cardioverter Defibrillators (ICDs):
    - PPMs, ICDs, and leads can be adversely affected by ablation energy. It is important to refer to the device manufacturer's instruction for use prior to performing ablation procedures.
    - Do not apply ablation energy directly to a lead or to tissue immediately in contact with a lead because it could potentially damage the lead or lead function.
    - Temporarily reprogram the pacemaker or defibrillator per the manufacturer guidelines during ablation. The device could be damaged by the ablation procedure. Interrogate the device fully after the ablation per the manufacturer guidelines and reprogram to preoperative sensing and pacing parameters.
    - Program the ICD Tachy therapy to "Off" to prevent inappropriate shock and/or possible damage to the device from the ablation procedure. Remember to turn Tachy Therapy to "On" once ablation is complete.
    - Have temporary external sources of pacing and defibrillation available.
    - Perform a complete analysis of the implanted device function after ablation.
    - Fluoroscopic or appropriate imaging guidance and care must be taken during catheter advancement, manipulation, and withdrawal to avoid lead dislodgement.
    - Monitor pre- and post-measurements for sensing and pacing thresholds and impedances to determine the integrity of the lead-patient function.
- Ablation in contact with any other electrodes alters the function of the catheter and can lead to embolism.
- At no time should a FARAWAVE Catheter be advanced, withdrawn, rotated, deployed or undeployed when resistance is felt, without determining the cause. Valve damage, vascular and/or cardiac perforation is a risk with any intracardiac catheter.
- Catheter entrapment within the heart or blood vessels is a possible complication of cardiac ablation procedures. The potential for catheter entrapment may be increased when the catheter is over torqued and/or positioned in the chordae tendineae. The occurrence of this complication may necessitate surgical intervention and/or repair of injured tissue and/or valve damage.
- Do not use the FARAWAVE Catheter in the proximity of Magnetic Resonance Imaging (MRI) equipment because the MRI equipment may adversely impact the function of a PFA Generator and the ablation system may adversely impact the image quality. This can also lead to loss of visibility during ablation which can cause patient injuries such as perforation, heart block and injury to adjacent structures.
- Catheter ablation procedures present the potential for significant radiation exposure, which can result in acute radiation injury as well as an increased risk for somatic and genetic effects, to both patients and laboratory staff due to the radiation beam intensity and duration of the fluoroscopic imaging. Catheter ablation should only be performed after adequate attention has been given to the potential radiation exposure associated with the procedure, and steps have been taken to minimize this exposure. Due to radiation exposure during catheter ablation, the safety and effectiveness of this device has not yet been established in pregnant and/or nursing women and pediatric patients.
- There are no data to support the safety and effectiveness of this device in the pediatric population.
- Prior to the procedure, always identify the patient's risk of volume overload. Monitor the patient's fluid

balance throughout the procedure and after the procedure to avoid fluid volume overload. Some patients may have factors that reduce their ability to handle the volume overload, making them susceptible to developing pulmonary edema or heart failure during or after the procedure. Patients with congestive heart failure or renal insufficiency, and the elderly are particularly susceptible.

- Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism.
- Excessive curves or kinking of the catheter may damage internal wires and components, including the flush lumen. This damage may affect mechanical and electrical performance leading to patient injury.
- Do not attempt to bend, kink, or shape the patient-contact portions or flush lumen of the FARAWAVE Catheter. Doing so could cause electrical or mechanical catheter failure resulting in patient injury. Kinking of the flush lumen may compromise flow through the device leading to potential thrombus formation and embolism.
- Use both fluoroscopy, or other visualization techniques such as echocardiography, and intracardiac electrograms to monitor the advancement and navigation of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade. Do not rely solely on electromagnetic navigation system display to monitor catheter location.
- The FARAWAVE Catheter tip and guidewire move forward during device undeployment. Device deployment and undeployment should be visualized using fluoroscopy. Failure to do so may result in catheter damage and/or patient injury.
- Do not deliver ablation energy with the catheter outside the target site. Ablation Generators can deliver significant electrical energy and may cause patient injury such as arrhythmia and heart block.
- Always verify that the tubing set, catheter, sheath and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing, catheter or sheath can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system.
- Patients undergoing left-sided ablation procedures should be closely monitored during and post procedure for clinical manifestations of myocardial infarction, pulmonary vein injury, nerve damage, and/or embolism.
- Patients undergoing an ablation procedure have the potential for greater anticoagulation and therefore Activated Coagulation Time (ACT) should be monitored closely due to the increased risk for bleeding/ hemorrhage and/or embolism.
- Patients with hemodynamic instability or cardiogenic shock are at increased risk for life-threatening adverse events and ablation must be done with extreme caution.
- The FARAWAVE Catheter is not intended to be used for internal cardioversion. Doing so may result in perforation, arrhythmias, embolism, thrombus and/or patient death.
- Inspect irrigation saline for air bubbles and remove any air bubbles prior to its use in the procedure. Air bubbles in the irrigation saline may cause embolism.
- If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, there should be a low threshold to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/or thrombus in the left atrial appendage.
- Guiding catheters and/or long introducer sheaths present the potential for thromboembolic events. Pre-flush and maintain lumen patency with heparinized intravenous infusion.
- Do not wipe this catheter with organic solvents such as alcohol or immerse the handle and/or cable connector in fluids. This may result in electrical or mechanical catheter failures. It may also result in an allergic reaction from the patient.
- Pre-procedural anticoagulation therapy is at the discretion of the physician. However, patients with a history of thromboembolic events may require therapeutic anticoagulation therapy, pre-, during and post-ablation to reduce the incidence of major complications. Peri-procedural anticoagulation therapy is recommended for patients undergoing left-sided and transseptal cardiac procedures and should be considered for selected patients undergoing right-sided procedures.
- The safety and/or efficacy of epicardial use of the FARAWAVE Catheter has not been evaluated in a clinical trial.
- Care should be used during multiple sheath/catheter exchanges through the transseptal puncture to avoid causing a residual atrial septal defect that would require repair.

- Do not leave the FARAWAVE Catheter in the patient for more than four (4) hours. Failure to remove the device before four hours after first insertion could result in formation of thrombus with increased thromboembolic risk.
- Use of the FARAWAVE Catheter with delivery devices other than the FARADRIVE Sheath can result in poor access to endocardial locations, inefficient ablation delivery and inadequate procedural outcomes.
- Cardiac ablation has the potential of causing unintended myocardial injury. Clinical indications of myocardial ischemia should be closely monitored during the procedure (e.g., ECG changes).
- The FARAWAVE Catheter has not been studied clinically for ablation in the mitral isthmus or cavotricuspid isthmus areas. Ablations in areas adjacent to coronary arteries may lead to coronary artery spasm and/or injury, and the resulting myocardial injury can be fatal.
- Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.
- When positioning on cardiac structures, the guidewire should be retracted to prevent cardiac perforation or tissue damage. Ensure the tip of the device is not against tissue prior to advancing or retracting the guidewire to prevent cardiac perforation or tissue damage.
- The risk of igniting flammable gases or other materials is potential outcome of ablation procedures. Precautions must be taken to restrict flammable materials from the electrosurgical suite.
- Take care when manipulating the guidewire to prevent cardiac or vessel trauma.
- To avoid cardiac damage, do not use excessive force when manipulating the catheter in vivo. Specifically, use caution when maneuvering while undeployed. Note that mapping and recording data do not require the use of force on the tissue.
- Minimize catheter exchanges and always advance and withdraw components through the valve slowly to minimize the vacuum created during withdrawal and to reduce the risk of air embolism. Follow advancement or withdrawal of catheters with appropriate aspiration and flushing according to institutional standards or consensus statements.
- Instruct users with co-implanted devices to refer to ancillary device labeling as well as the manufacturer of the ancillary device for recommended compatibility and settings. When ablating in proximity to metallic devices, arcing may occur which could lead to bubble formation, cardiac trauma, and/or damage to the devices.
- Use caution when advancing, retracting or otherwise manipulating system components to avoid damaging tissue or vessels or interfering with previously implanted medical devices.
- When advancing or undeploying the FARAWAVE catheter, do not retract the guidewire simultaneously. If resistance is felt during retraction of the guidewire, do not continue to retract the guidewire until cause of resistance is determined as this may result in cardiac trauma. If resistance is felt, it may be necessary to advance guidewire under imaging guidance before continuing to retract.
- Ensure that the guidewire is not contacting ablation electrodes prior to starting ablation to prevent inappropriate energy delivery.
- Always un-deploy the catheter and withdraw the catheter into the sheath before removing the catheter from the Left Atrium (LA). Deploying the catheter in the septal puncture site or crossing the septum while the catheter is unsheathed or deployed may cause serious atrial septal defects or other cardiac and vessel trauma. Use visualization (such as fluoroscopy) to verify undeployment.
- Avoid deploying the catheter in constrained parts of the anatomy to prevent cardiac trauma or damage to the device.
- Prior to starting ablation verify that the catheter has been positioned and deployed correctly to prevent inappropriate application of ablation energy.
- Do not deploy the catheter while the distal end is inside the sheath as it could lead to catheter damage which may result in patient harm.
- Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed in the Operational Instructions section, regardless of absence of intracardiac signal.

- Operation of the FARAPULSE PFA System may cause transient intravascular hemolysis, which may manifest as hemoglobinuria. In order to reduce the risk of clinical sequelae of intravascular hemolysis, it is recommended to adhere to the nominal workflow per the IFU. Consider the application of additional ablations per physician judgment taking into account patient condition including hydration status, anatomy, and available clinical evidence with FARAPULSE PFA System. Evaluate the patient's risk tolerance for hemoglobinemia and related sequelae prior to the procedure. Consider hydration prior to, during, and post-procedure.
- Potential biohazard after use. Handle and dispose of in accordance with applicable regulations.

PRECAUTIONS

- Do not attempt to use with devices, including guidewires, larger than the delivery lumen diameter specified on the package label.
- Care must be taken to ensure all luer fittings are secure to prevent leaking.
- It is essential that a cardiac defibrillator with paddles connected is readily available in the procedure room for use if Ventricular Fibrillation is noted subsequent to ablation.
- Catheter deployment and undeployment should occur under imaging guidance. Catheter may be fully deployed or undeployed even though the slider switch is not fully engaged. Failure to monitor deployment may result in catheter damage and need for catheter exchange.
- Device deployment friction is increased when attempting to deploy the device when the catheter shaft is bent. FARAWAVE Catheter deployment should always occur with the catheter shaft as straight as possible.
- Do not apply excessive force to the deployment mechanism when deploying the catheter as doing so may damage the catheter.
- Avoid allowing the distal end of the catheter to be put into an acute bend, particularly when advancing the catheter beyond the sheath or deploying the catheter. A catheter exchange may be necessary if the catheter deploys improperly.
- Do not place the distal end of the catheter near a magnet. Magnetization of the catheter may result in degradation of magnetic tracking precision. Such degradation may be manifested by an unstable or complete loss of rendering of the position and/or orientation of the catheter by a magnetic tracking system. If this occurs, the catheter should be replaced.

ADVERSE EVENTS

Potential adverse events associated with use of the FARAWAVE Catheter includes, but are not limited to:

- Pain or discomfort, for example:
  - Angina
  - Chest pain
  - Non-cardiovascular pain
- Cardiac arrest
- Death
- Electric shock
- Hypotension
- Infection/inflammation/exposure to biohazardous material
- Pulmonary edema/heart failure/pleural effusion
- Hemolysis
- Renal failure/insufficiency
- Respiratory distress/insufficiency/dyspnea
- Arrhythmia (new or exacerbated)
  - Conduction pathway injury (for example: heart block, injury to sinus or AV node, etc.)
- Nerve injury, for example:
  - Phrenic nerve injury
  - Vagal nerve injury

- Gastrointestinal disorders
- Vessel trauma, including:
  - Perforation
  - Dissection
  - Coronary artery injury
  - Vasospasm
  - Occlusion
  - Hemothorax
- Cardiac trauma, for example:
  - Cardiac perforation/cardiac tamponade/pericardial effusion
  - Valvular damage
  - Stiff left atrial syndrome
- Injury related to tissue damage and/or adjacent structures, for example:
  - Esophageal injury
  - Pulmonary injury
  - Catheter entrapment
  - Physical trauma
- Fistula, for example:
  - Atrio-esophageal fistula
  - Bronchopericardial fistula
- PV stenosis and its symptoms, for example:
  - Cough
  - Shortness of breath, fatigue
  - Hemoptysis
- Surgical and access site complications, for example:
  - Hematoma/seroma
  - AV fistula
  - Bleeding
  - Pseudoaneurysm
  - Pneumothorax
  - Residual atrial septal defect
- Thrombus/thrombosis
- Muscle spasm
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
  - Cerebrovascular Accident (CVA)/stroke
  - Transient Ischemic Attack (TIA)
  - Myocardial infarction
  - Neurological impairment and its symptoms, for example:
    - Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment
  - Pulmonary embolism
  - Peripheral embolism
  - Asymptomatic cerebral embolism
- Procedural related side effects, for example:
  - Allergic reaction (including anaphylaxis)
  - Genitourinary complication

- Side effects related to medication or anesthesia
- Radiation injury/tissue burn
- Vasovagal response
- Fluid volume overload

The potential adverse events may be related to the ablation catheter(s) and/or the interventional procedure. The severity and/or the frequency of these potential adverse events may vary and may result in prolonged procedure time and/or additional medical and/or surgical intervention, implantation of a permanent device such as a pacemaker, and in rare cases, may result in death.

CLINICAL STUDIES

ADVENT Clinical Study

Study Title	The ADVENT Trial – A Prospective Randomized Pivotal Trial of the FARAPULSE Pulsed Field Ablation System Compared with Standard of Care Ablation in Patients with Paroxysmal Atrial Fibrillation
Number of Centers	30 sites in the United States
Number of Subjects	706 enrollments, including 80-roll-in subjects and 626 randomized subjects (313 Pulsed Field and 313 Thermal [171 Radiofrequency (RFA) ablation, 142 Cryoballoon (CBA)]). 19 subjects withdrew prior to the procedure resulting in 607 modified-intent-to-treat (MITT) subjects (305 Pulsed Field and 302 Thermal [167 RF ablation and 135 CBA]).

Objective

The primary objective of the ADVENT Trial was to establish valid scientific evidence that endocardial ablation using the FARAPULSE Pulsed Field Ablation System is both safe and effective for treating patients with drug-resistant, recurrent, symptomatic paroxysmal atrial fibrillation (PAF).

Design, Scope, and Methods

The ADVENT Trial was a prospective, Bayesian adaptive, multi-center, 1:1 randomized, blinded, non-inferiority safety and effectiveness pivotal study comparing the FARAPULSE Pulsed Field Ablation System with thermal ablation (using either force-sensing RFA catheters or CBA catheters) for the treatment of patients with drug-resistant, recurrent, symptomatic PAF. All subjects who met the eligibility criteria, signed the informed consent, and underwent the Index Procedure were followed for 12 months post-ablation with weekly event monitoring beginning on Day 90, and 72-hour Holter monitoring at Months 6 and 12. Clinical follow-up at Days 7, 30, 90, Month 6 and Month 12 were performed to determine any occurrence of adverse events or arrhythmia recurrence.

Endpoints

Primary Safety Endpoint

The primary safety endpoint was the Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device- or procedure-related SAEs as adjudicated by the Clinical Events Committee (CEC) according to the protocol-specified definitions.

Early onset

Any of the following with an Onset Date within 7 days of the Index / Rescheduled Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation
- Pericarditis
- Pulmonary edema
- Vascular access complications

- Heart block
- Gastric motility/pyloric spasm disorders

Late onset

Either of the following with an Onset Date any time through the completion of 12-month follow-up visit:

- Pulmonary Vein Stenosis
- Atrio-esophageal fistula

Hypothesis

The analysis of the primary safety endpoint was a test of non-inferiority of the event rate at 12 months using a non-inferiority margin of 8%. The null and alternative hypotheses are presented below for primary safety:

$H_0: Q_T \geq Q_C + 0.08$ versus $H_A: Q_T < Q_C + 0.08$

where QT is the CSE proportion in the Pulsed Field (Treatment) Group and QC is the CSE proportion in the Thermal (Control) Group. The differences in the proportion of subjects with 1 or more CSE events between the Pulsed Field Group and the Thermal Group will be tested with a Bayesian statistical method and the prior distributions for QT and QC in these calculations are Beta (0.5, 0.5), which is the Jeffreys non-informative prior. QT will be deemed to be non-inferior to QC if it can be established that the posterior probability Pr(HA | data) > Ψsaf, where Ψsaf is a pre-specified threshold value that controls the one-sided type I error rate (under simulation) at level 0.05.

Primary Effectiveness Endpoint

The Primary Effectiveness Endpoint was Treatment Success in MITT subjects through the Month 12 Assessment, defined as:

1. Acute Procedural Success, defined as demonstration of isolation of all attempted PVs using the randomized treatment during the first ablation procedure as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing and
2. Chronic Success, defined as freedom from:
   a. Use of a non-randomized treatment modality for PVI at the Index Procedure and
   b. After the Blanking Period, occurrence of any detectable atrial fibrillation (AF), atrial flutter (AFL) or atrial tachycardia (AT)[1], any cardioversion for AF, AFL or AT, use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT and
   c. At any time, re-ablation for AF, AFL or AT (other than for CTI-dependent flutter) or use of amiodarone, except intra-procedurally to control an arrhythmia

Hypothesis

The primary effectiveness endpoint for this study was Treatment Success, which will be analyzed as a test of non-inferiority of the event rate at 12 months using a non-inferiority margin of 15%. The null and alternative hypotheses are:

$H_0: P_T \leq P_C - 0.15$ versus $H_A: P_T > P_C - 0.15$

where PT is the Treatment Success rate at 12 months in the Pulsed Field Group and PC is the Treatment Success rate at 12 months in the Thermal (Control) Group.

This study was designed using Bayesian statistical techniques and the prior distributions for PT and PC in these calculations are Beta (0.5, 0.5), which is the Jeffreys non-informative prior. PT will be deemed to be non-inferior to PC if it can be established that the posterior probability Pr(HA | data) > Ψeff, where Ψeff is a pre-specified threshold value that controls the one-sided type I error rate (under simulation) at level 0.05.

Subject Accountability

All subjects who signed and dated the Informed Consent Form were considered enrolled in the study. Subjects were classified as either Roll-In or Randomized:

- **Roll-In Subject** – To help facilitate Investigators' familiarity with the new investigational system and avoid learning curve bias, the first 1-3 subjects at each site were enrolled as Roll-In subjects. Data from Roll-In subjects are not included in the endpoint analyses or results presented.

1 Detectable AF, AFL or AT is an episode of AF, AFL or AT which is permanently recorded for review, contains at least 30 seconds of continuous interpretable signal, includes symptomatic and asymptomatic episodes, and excludes CTI isthmus-dependent AFL when the mechanism is confirmed electrophysiologically

- **Randomized Subject** – Once roll-in requirements were satisfied, all subsequent subjects enrolled were randomized 1:1 to receive either Pulsed Field ablation or Thermal (control) ablation. Thermal control modality (RFA or CBA) was determined at the site level. Subject classification was as follows:
  - **Intent-to-Treat (ITT)** – Enrolled subjects randomized to either the Pulsed Field group or Thermal group.
  - **Modified Intent-to-Treat (MITT)** – ITT subjects who received any energy delivery for pulmonary vein isolation (PVI) with the randomized ablation catheter the Index Procedure.

A total of 706 subjects were enrolled in the study, including 80 Roll-In subjects and 626 Randomized subjects, 313 in the Pulsed Field Group and 313 in the Thermal Group (171 RFA, 142 CBA). Nineteen (19) subjects (8 PFA, 11 Thermal) exited the study prior to undergoing the Index Procedure ablation, resulting in 607 Randomized subjects in the MITT cohort (305 Pulsed Field, 302 Thermal [167 RFA and 135 CBA]). Of the 607 MITT subjects, 583 (96.0%) completed the 12-month follow-up (293 PFA subjects and 290 Thermal subjects), with the 24 early exits equally represented across the groups (12 Pulsed Field, 12 Thermal).

Study Population Demographics, Baseline Parameters, and Visit Compliance

Effective randomization was verified by comparing the groups on basic demographic data, assessments of AF status, and multiple cardiovascular parameters. Key baseline comparators for the MITT subjects are presented in Table 2 and Table 3. While there were a few statistical differences between the Pulsed Field and Thermal groups, commonly seen when multiple comparisons are performed, none were clinically significant.

Table 2. Baseline Demographics and Arrhythmia History – MITT Subjects

Baseline Perimeter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[1]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
Female	34.6 (210/607)	33.8 (103/305)	[-9.2, 5.9]	35.4 (107/302)	32.9 (55/167)	38.5 (52/135)
Male	65.4 (397/607)	66.2 (202/305)		64.6 (195/302)	67.1 (112/167)	61.5 (83/135)
Hispanic or Latino	1.8 (11/607)	2.6 (8/305)	[-0.5, 4.0]	1.0 (3/302)	1.2 (2/167)	0.7 (1/135)
White	91.9 (558/607)	93.8 (286/305)	[-0.6, 8.1]	90.1 (272/302)	89.8 (150/167)	90.4 (122/135)
Black/African American	2.5 (15/607)	1.3 (4/305)	[-5.0, 0.1]	3.6 (11/302)	4.2 (7/167)	3.0 (4/135)
Asian	1.8 (11/607)	2.0 (6/305)	[-1.9, 2.6]	1.7 (5/302)	1.2 (2/167)	2.2 (3/135)
American Indian or Alaska Native	0.2 (1/607)	0.0 (0/305)	[-1.4, 0.5]	0.3 (1/302)	0.6 (1/167)	0.0 (0/135)
Native Hawaiian or other Pacific Islander	0.5 (3/607)	0.3 (1/305)	[-1.7, 0.9]	0.7 (2/302)	1.2 (2/167)	0.0 (0/135)
Race Unknown	1.5 (9/607)	0.7 (2/305)	[-3.8, 0.2]	2.3 (7/302)	1.8 (3/167)	3.0 (4/135)
Race Not Specified	1.6 (10/607)	2.0 (6/305)	[-1.5, 2.8]	1.3 (4/302)	1.2 (2/167)	1.5 (2/135)
Typical Atrial Flutter	30.1 (183/607)	27.2 (83/305)	[-13.1, 1.4]	33.1 (100/302)	42.5 (71/167)	21.5 (29/135)
Other SVT	14.0 (85/607)	11.8 (36/305)	[-10.0, 1.1]	16.2 (49/302)	21.0 (35/167)	10.4 (14/135)

Baseline Perimeter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[1]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
Previous RA Ablation	3.9 (22/562)	3.5 (10/283)	[-4.1, 2.5]	4.3 (12/279)	5.0 (8/161)	3.4 (4/118)

Note 1: Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors.

Table 3. Baseline Demographics and Medical History – MITT Subjects

Baseline Perimeter	Total Subjects Mean (N) Min, Max	Pulsed Field Subjects Mean (N) Min, Max	95% BCI[1]	Thermal Subjects Mean (N) Min, Max	RFA Subjects Mean (N) Min, Max	CBA Subjects Mean (N) Min, Max
Age (years)	62.4 (607) 30, 75	62.4 (305) 36, 75	[-1.5, 1.3]	62.5 (302) 30, 75	62.5 (167) 42, 75	62.4 (135) 30, 75
Height (cm)	175.7 (607) 147, 201	175.9 (305) 147, 198	[-1.0, 2.2]	175.4 (302) 149, 201	176.3 (167) 149, 201	174.2 (135) 149, 196
Weight (kg)	88.7 (607) 45.4, 145.6	87.9 (305) 45.4, 137.9	[-4.5, 1.1]	89.6 (302) 45.6, 145.6	89.0 (167) 45.6, 136	90.3 (135) 47.6, 145.6
BMI	28.7 (607) 15, 47.2	28.3 (305) 15, 41.6	[-1.45, 0.05]	29.0 (302) 17.7, 47.2	28.5 (167) 17.7, 47.2	29.6 (135) 18.6, 40
LVEF (%)	60.1 (600) 40, 78	60.5 (300) 40, 78	[-0.1, 1.9]	59.6 (300) 40, 77	60.6 (167) 40, 77	58.4 (133) 44, 75
Left Atrial Diameter (mm)	39.2 (607) 23, 55	38.8 (305) 23, 55	[-1.6, 0.2]	39.6 (302) 24, 54	39.3 (167) 24, 53	40.0 (135) 25, 54
Years since first AF diagnosis	3.6 (607) 0, 51.55	3.8 (305) 0, 51.55	[-0.4, 1.4]	3.3 (302) 0, 36.19	3.5 (167) 0, 21.65	3.1 (135) 0, 36.19

Baseline Perimeter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[2]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
CAD	13.7 (83/607)	10.5 (32/305)	[-11.9, -0.9]	16.9 (51/302)	17.4 (29/167)	16.3 (22/135)
Diabetes	10.7 (65/607)	10.8 (33/305)	[-4.7, 5.2]	10.6 (32/302)	11.4 (19/167)	9.6 (13/135)
CHF: NYHA Class I or II	19.4 (118/607)	19.3 (59/305)	[-6.5, 6.1]	19.5 (59/302)	18.6 (31/167)	20.7 (28/135)
Sleep Apnea	27.8 (169/607)	26.6 (81/305)	[-9.7, 4.6]	29.1 (88/302)	28.7 (48/167)	29.6 (40/135)
Using CPAP	77.5 (131/169)	71.6 (58/81)	[-23.8, 1.2]	83.0 (73/88)	79.2 (38/48)	87.5 (35/40)
CHA_2DS_2-VASc Score	1.7 (606) 0, 6	1.7 (304) 0, 6	[-0.2, 0.2]	1.7 (302) 0, 6	1.8 (167) 0, 5	1.6 (135) 0, 6

Note 1: Bayesian credible interval for the difference in means, using uniform priors on (μ, log(σ)) scale.
Note 2: Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors.

Follow-up visit compliance (pre-discharge, Day 7, Day 90, Month 6, and Month 12) was high and similar across both treatment groups with an overall compliance rate of 99.3% in the Pulsed Field group (1800/1813) and 99.3% (1786/1799) in the Thermal group. Post-ablation rhythm monitoring for the MITT cohort included symptomatic and weekly event monitor transmissions during the evaluation period, 12-lead ECGs at Day 90 and 12 months, and 72-Hour Holter monitors at 6-months and 12-months post-Index Procedure. Overall rhythm monitoring compliance across all

assessment methods was 70.0% (71.3% Pulsed Field and 68.7% Thermal).

Procedural Durations

The duration of clinically relevant portions of each Index Procedure were recorded and compared descriptively. Procedure time (mean 105.8 versus 123.1 minutes), LA dwell time (mean 59.4 versus 83.7 minutes), total ablation time (mean 29.2 versus 50.0 minutes), and pre-ablation mapping time (mean 3.8 versus 6.2 minutes) were all significantly different and shorter in the Pulsed Field group as compared to the Thermal group. Fluoroscopy time was longer in the Pulsed Field group (mean 21.1 versus 13.9 minutes), as many thermal procedures have shifted to fluoroless procedures, which is further enabled by the integrated mapping system technologies that were used. Procedure times were inclusive of the protocol-required 20-minute wait, CTI ablation time, and any additional ablation, if performed.

Results

Primary Safety Endpoint

The primary safety endpoint was the CSE defined as the proportion of MITT subjects with one or more pre-specified device- or procedure-related SAEs adjudicated by the ADVENT Clinical Events Committee. The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a Bayesian test of non-inferiority of the CSE rate at 12 months using a non-inferiority margin of 8%.

In Pulsed Field MITT subjects, six (6) subjects experienced one or more CSE events; the estimated incidence was 2.1% (posterior mean). In Thermal MITT subjects, four (4) subjects experienced one or more CSE events; the estimated incidence was 1.5% (posterior mean).

The ADVENT Trial met the success criterion for the primary safety endpoint. The probability of a Pulsed Field MITT subject having one or more CSE events was non-inferior to the probability of a Thermal MITT subject having one or more CSE events using a non-inferiority margin of 8%: the posterior probability of non-inferiority was >0.999, which exceeded the pre-specified threshold of 0.966 (Table 4).

Table 4. Primary Safety Endpoint – MITT Subjects

Primary Safety Endpoint	Subjects with Events (N) Incidence (%) 95% BCI[1]		Difference (%) 95% BCI[2]	Posterior Probability of Non-Inferiority (δ = 8%)[3]
	Pulsed Field Group N = 305	Thermal Group N = 302		
MITT Subjects with one or more CSE events	6 2.1 [0.8, 4.0]	4 1.5 [0.4, 3.1]	0.6 [-1.5, 2.8]	> 0.999

Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.
Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.
Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

The components of the CSE Events were analyzed as separate outcomes in Table 5. Six (6) Pulsed Field subjects experienced a CSE, of the following types: 1 death, 1 TIA, 2 cardiac tamponade/ perforation, 1 pericarditis, 1 pulmonary edema, and 1 vascular access complication. One subject in the Pulsed Field group experienced two events (death and cardiac tamponade/perforation). Four (4) subjects in Thermal group experience a CSE: 1 stroke, 1 pulmonary edema, and 2 vascular access complications. All CSEs in the Thermal group occurred in RFA subjects.

Table 5. Proportion of MITT Subjects with One or More CSE Events by Event Type

MITT Subjects with One or More CSE Events by Event Type	Pulsed Field Group[1] % (n / N)	Thermal Group % (n / N)
Any CSE Event	**2.0 (6/305)**	**1.3 (4/302)**
Death	0.3 (1/305)	0.0 (0/302)
Myocardial infarction	0.0 (0/305)	0.0 (0/302)
Persistent phrenic nerve palsy	0.0 (0/305)	0.0 (0/302)
Stroke	0.0 (0/305)	0.3 (1/302)

MITT Subjects with One or More CSE Events by Event Type	Pulsed Field Group[1] % (n / N)	Thermal Group % (n / N)
TIA	0.3 (1/305)	0.0 (0/302)
Peripheral organ thromboembolism	0.0 (0/305)	0.0 (0/302)
Cardiac tamponade or perforation	0.7 (2/305)	0.0 (0/302)
Pericarditis	0.3 (1/305)	0.0 (0/302)
Pulmonary edema	0.3 (1/305)	0.3 (1/302)
Vascular access complication	0.3 (1/305)	0.7 (2/302)
Heart block	0.0 (0/305)	0.0 (0/302)
Gastric motility/ pyloric spasm	0.0 (0/305)	0.0 (0/302)
Pulmonary vein stenosis	0.0 (0/305)	0.0 (0/302)
Atrio-esophageal fistula	0.0 (0/305)	0.0 (0/302)

Abbreviations: n = number of subjects with event, N = number of evaluable subjects.

Note 1: PFA Subject 109-017 has event meeting the CSE definition for both death and cardiac tamponade/perforation and is included in event counts for both CSE events

Secondary Safety Endpoint

The secondary safety endpoint was Aggregate PV Cross-Sectional Area, defined as the paired difference in the computed Aggregate PV Cross-Sectional Area between baseline and 3 months in MITT subjects. This was compared between randomization groups, regardless of re-ablation with any second energy modality. The within-subject changes in the Aggregate PV Cross-Sectional Area from baseline to Day 90 were tested between the Pulsed Field and Thermal Groups for superiority (less reduction in area) using a Bayesian version of a t-test.

The secondary safety endpoint success criterion for superiority was met. The mean change in PV cross-sectional area in Pulsed Field MITT subject PVs (–0.18 cm^2 or -0.9% of baseline value) was statistically less than the change in Thermal MITT subject PVs (–1.18 cm2 or -12.0% of baseline value) with an observed posterior probability of >0.999, exceeding the prespecified threshold value of 0.975 (Table 6).

Examination of the change in Aggregate PV Cross-Sectional Area by ablation modality demonstrated that the difference was driven by the large reduction in RFA subjects, who had a mean reduction of 19.5% in Aggregate PV Cross-Sectional Area. Thermal subjects treated with CBA had a 3.3% reduction.

Table 6. Aggregate PV Cross-Sectional Area by Ablation Modality

Aggregate PV Cross-Sectional Area (cm^2)	Interval	Pulsed Field Subjects Mean (N) Min, Max	Thermal Group		
			All Thermal Subjects Mean (N) Min, Max	RFA Subjects Mean (N) Min, Max	CBA Subjects Mean (N) Min, Max
MITT Subjects	Baseline	8.9 (259) 3.7, 15.3	8.9 (255) 4.0, 17.6	9.1 (137) 5.0, 17.6	8.7 (118) 4.0, 15.7
	Day 90	8.7 (259) 4.2, 15.1	7.8 (255) 3.6, 13.5	7.3 (137) 3.6, 12.4	8.3 (118) 3.7, 13.5
	Percent Change	-0.9 (259) -40.7, 65.5	-12.0 (255) -55.2, 44.3	-19.5 (137) -55.2, 16.8	-3.3 (118) -44.5, 44.3
	Change [95% BCI][1]	-0.18 [-0.37, 0.00]	-1.18 [-1.39, -0.97]	-1.86 [-2.12, -1.59]	-0.39 [-0.67, -0.11]
	Posterior Mean of Difference 95% BCI[2]	1.00 [0.72, 1.28]			
	Posterior Probability of Superiority[3]	>0.999			

Note 1: This change is the paired comparisons of the baseline to Day 90 mean values within each treatment group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log(s)) scale

Note 2: This difference is the comparison of the baseline to Day 90 change in per-subject means between PFA and Thermal group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log(σ)) scale.

Note 3: Posterior probability that the change in baseline to Day 90 mean values is larger (less negative) in the Pulsed Field group than the Thermal group, using a Bayesian version of a t-test; uniform priors on (μ, log(σ)) scale.

Additional Safety Information

There were no Unanticipated Adverse Device Effects (UADEs) in the ADVENT Trial.

Summary of Clinical Trial Adverse Events

The following table summarizes the incidence of all major categories of adverse events, comparing the MITT subjects in the Pulsed Field and the Thermal Groups. There were no statistical differences in any adverse events or SAEs, any procedure- or device-related AEs, between the two groups. There were 20 Pulsed Field subjects with one or more procedure-related SAEs compared with 9 Thermal subjects, a statistical difference presented in the table below. The device-related SAEs are all included within the procedure-related numbers.

Table 7. Overview of Adverse Events – MITT Subjects

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	95% BCI[2]	Thermal Subjects (N = 302) n (%) e[1]	RFA Subjects (N = 167) n (%) e[1]	CBA Subjects (N = 135) n (%) e[1]
Any adverse event	390 (64.3%) 1012	189 (62.0%) 487	[-12.2, 3.0]	201 (66.6%) 525	115 (68.9%) 321	86 (63.7%) 204
Any SAE	71 (11.7%) 103	37 (12.1%) 51	[-4.3, 6.0]	34 (11.3%) 52	21 (12.6%) 37	13 (9.6%) 15
Any procedure-related AE	191 (31.5%) 288	97 (31.8%) 147	[-6.7, 8.0]	94 (31.1%) 141	58 (34.7%) 89	36 (26.7%) 52
Any device-related AE	40 (6.6%) 45	21 (6.9%) 22	[-3.4, 4.6]	19 (6.3%) 23	13 (7.8%) 16	6 (4.4%) 7
Any procedure-related SAE	29 (4.8%) 34	20 (6.6%) 23	[0.2, 7.1]	9 (3.0%) 11	7 (4.2%) 9	2 (1.5%) 2
Any device-related SAE	4 (0.7%) 4	4 (1.3%) 4	[0.1, 3.0]	0 (0.0%) 0	0 (0.0%) 0	0 (0.0%) 0

Note 1: N = number of subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Note 2: Bayesian credible interval of the difference in proportions of subjects with one or more events using Beta (0.5, 0.5) priors

Serious Adverse Events

All adverse events reported were screened by the CEC per the protocol requirements and CEC charter. Events reported as serious, and additional events that study monitors or CEC members felt might be serious, were all formally adjudicated by the CEC.

There were 34 device- or procedure-related SAEs reported in 29 subjects (20 Pulsed Field and 9 Thermal). Eleven (11) of the events in ten (10) subjects were the primary safety endpoint events presented previously in the primary safety endpoint results. The remaining 23 events (16 Pulsed Field and 7 Thermal) are summarized in Table 8 below. All of these SAEs were determined to be resolved (21) events or resolving (2 events) by the conclusion of study participation without reported sequelae.

Table 8. Related Serious Adverse Events by Category – MITT Subjects

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	Thermal Subjects (N = 302) n (%) e[1]	95% BCI[2]
Total Device or Procedure Related Serious Adverse Events	**29 (4.8%) 34**	**20 (6.6%) 23**	**9 (3.0%) 11**	**[0.2, 7.1]**
Atrial Flutter	3 (0.5%) 4	2 (0.7%) 3	1 (0.3%) 1	[-1.0, 1.7]

Adverse Event	All Subjects (N = 607) n (%) e[1]	Pulsed Field Subjects (N = 305) n (%) e[1]	Thermal Subjects (N = 302) n (%) e[1]	95% BCI[2]
Atypical (Type II) Atrial Flutter	2 (0.3%) 3	1 (0.3%) 2	1 (0.3%) 1	[-1.2, 1.2]
Pseudoaneurysm	3 (0.5%) 3	1 (0.3%) 1	2 (0.7%) 2	[-1.7, 0.9]
Myocardial Perforation With Tamponade	2 (0.3%) 2	2 (0.7%) 2	0 (0.0%) 0	[-0.3, 2.0]
Oozing/Bleeding	2 (0.3%) 2	2 (0.7%) 2	0 (0.0%) 0	[-0.3, 2.0]
Procedure Related Genitourinary	2 (0.3%) 2	1 (0.3%) 1	1 (0.3%) 1	[-1.2, 1.2]
Pulmonary Edema	2 (0.3%) 2	1 (0.3%) 1	1 (0.3%) 1	[-1.2, 1.2]
Abnormal Lab Values	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Access Site Complication	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Atrial Fibrillation	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Atrial Flutter Not Specified	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Cerebral Vascular Accident	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Conduction Disturbances/Arrhythmia - Other	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
EP/Ablation Other-Multi Organ Failure	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Fistula (Arterial/Venous)	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Intracardiac Thrombus	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Left Atrial (Type II, Atypical) Atrial Flutter	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Pain Cardiovascular (Non-Ischemic)	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Pericarditis	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Procedure Related Hypertension	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Symptomatic Pericardial Effusion	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]
Systemic Infection	1 (0.2%) 1	0 (0.0%) 0	1 (0.3%) 1	[-1.4, 0.5]
Transient Ischemic Attack	1 (0.2%) 1	1 (0.3%) 1	0 (0.0%) 0	[-0.5, 1.4]

Note 1: N = number of subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Note 2: Bayesian credible interval of the difference in proportions of subjects with one or more events using Beta (0.5, 0.5) priors

Primary Effectiveness Endpoint

The primary effectiveness endpoint was Treatment Success (Acute Procedural Success and Chronic Success). The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a test of non-inferiority of the Treatment Success rate at 12 months using a non-inferiority margin of 15%.

In Pulsed Field MITT subjects, 204 subjects were Treatment Successes, while 80 subjects experienced Treatment Failures; the remaining 21 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 21 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment Success Rate is 73.3% (calculated as the mean of the posterior distribution).

In Thermal MITT subjects, 194 subjects were Treatment Successes, while 85 subjects experienced Treatment Failures; the remaining 23 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 23 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment Success Rate is 71.3% (calculated as the mean of the posterior distribution).

The ADVENT trial met the success criterion for the primary effectiveness endpoint. The probability of a Pulsed Field MITT subject having Treatment Success was non-inferior to the probability of a Thermal MITT subject having Treatment Success using a non-inferiority margin of 15%: the posterior probability of non-inferiority is >0.999, which exceeded the prespecified threshold of 0.956.

Table 9. Primary Effectiveness Endpoint – MITT Subjects

Primary Effectiveness Endpoint	Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] Incidence (%) 95% BCI[1]		Difference (%) 95% BCI[2]	Posterior Probability of Non-Inferiority (δ = 15%)[3]
	Pulsed Field Group N = 305	Thermal Group N = 302		
MITT Subjects with Treatment Success	204 [21] 73.3 [68.1, 78.1]	194 [23] 71.3 [66.0, 76.3]	2.0 [-5.2, 9.2]	> 0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

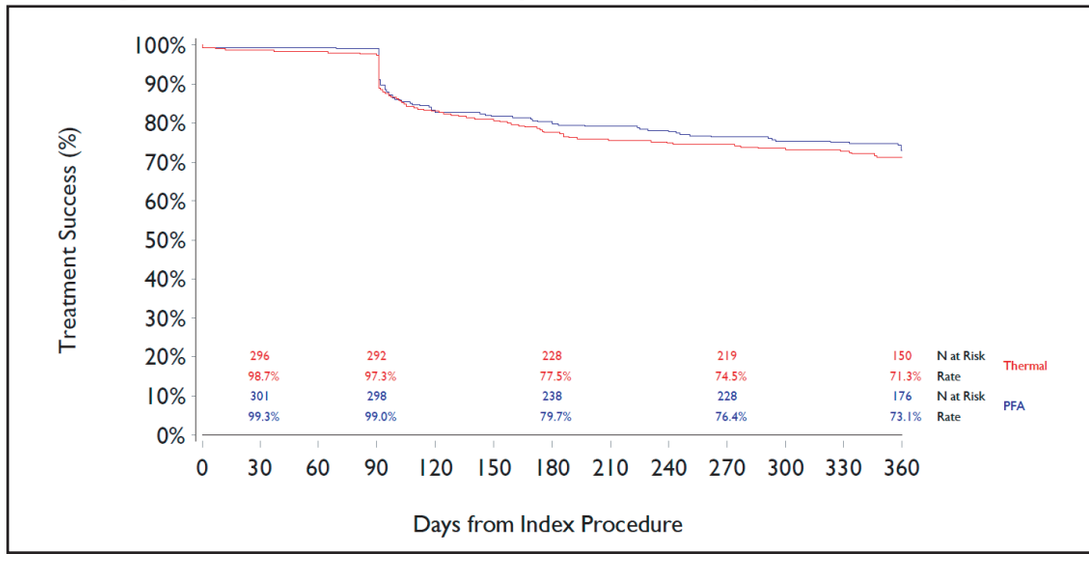
Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.

Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

As a sensitivity analysis, the primary effectiveness endpoint was also assessed via Kaplan-Meier estimates, as shown in Figure 2. The Kaplan-Meier estimate of freedom from failures of the primary effectiveness endpoint at 360 days is 73.1% in the Pulsed Field group and 71.3% in the Thermal group. Although freedom from failures at 360 days differs somewhat from the Treatment Success definition in that 12-month follow-up visits and their associated visit windows are not formally considered, the numerical estimates agree closely: 73.3% for Pulsed Field subjects and 71.3% for Thermal subjects from the pre-specified Bayesian model and 73.1% for Pulsed Field subjects and 71.3% for Thermal subjects from the Kaplan-Meier estimates.

Figure 2. Survival Analysis, Primary Effectiveness Endpoint – MITT Subjects



The mode of the earliest failure of the primary effectiveness endpoint for each MITT subject is detailed in the following table. The data show similar distributions of failure modes for the Pulsed Field and Thermal subjects.

Table 10. Earliest Primary Effectiveness Failure Modes – MITT Subjects

Earliest Primary Effectiveness Failure Modes	Pulsed Field Group N = 305 Incidence, %1 (Subjects with event)	Difference 95% BCI[1]	Thermal Group N = 302 Incidence, %[1] (Subjects with event)
Any Primary Effectiveness Failure Mode[2]	**26.7 (80)**	**-2.0 [-9.2, 5.2]**	**28.7 (85)**
Acute Procedural Failure	0.8 (2)	-0.0 [-1.5, 1.5]	0.8 (2)

Earliest Primary Effectiveness Failure Modes	Pulsed Field Group N = 305 Incidence, %1 (Subjects with event)	Difference 95% BCI[1]	Thermal Group N = 302 Incidence, %[1] (Subjects with event)
Post-blanking Detectable AF/AFL/AT	17.2 (51)	0.7 [-5.2, 6.7]	16.4 (48)
Post-blanking Detectable AF	11.2 (33)	1.2 [-3.7, 6.1]	10.0 (29)
Post-blanking Detectable AFL	4.8 (14)	-0.4 [-4.0, 3.1]	5.3 (15)
Post-blanking Detectable AT	1.5 (4)	-0.0 [-2.1, 2.0]	1.5 (4)
Post-blanking cardioversion for AF/AFL/AT	0.5 (1)	0.3 [-0.6, 1.5]	0.2 (0)
Post-blanking use of Type I/III AAD	8.1 (24)	-1.1 [-5.6, 3.4]	9.2 (27)
Re-ablation for AF/AFL/AT	0.5 (1)	-0.0 [-1.2, 1.2]	0.5 (1)
Any non-procedural use of amiodarone	0.5 (1)	-2.0 [-4.2, -0.2]	2.5 (7)

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note 1: Point estimate for incidence and incidence difference calculated as the mean of the relevant posterior distribution; posterior mean and Bayesian credible interval calculated Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors and multiple imputation for incomplete data.

Note 2: Each subject has only one earliest primary effectiveness failure mode.

Acute Procedural Success

Acute Procedural Success was defined as demonstration of Acute Vein Success in all attempted PVs using the randomized treatment catheter during the Index/Rescheduled Index Procedure, as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion was made, with or without adenosine.

The proportion of Pulsed Field MITT subjects with Acute Procedural Success was 99.3%, and the proportion of Thermal MITT subjects with Acute Procedural Success was 99.3%. There was not a statistical difference between these results [95% BCI -1.5, 1.5]. There were two acute procedural failures in the Pulsed Field group and two in the Thermal group.

Study Conclusion

The ADVENT Trial results constitute valid scientific evidence that gives reasonable assurance of the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System when used in the treatment of patients with drug-resistant, recurrent, symptomatic paroxysmal atrial fibrillation.

Supplemental Clinical Information: FARA-Freedom Post-Market Clinical Follow-Up Study

Study Title	A Prospective Open-Label Single Arm Post Market Clinical Follow-Up Trial of the FARAPULSE Pulsed Field Ablation System in Patients with Paroxysmal Atrial Fibrillation
Number of Centers	14 sites in Europe
Number of Subjects	180 subjects treated with the FARAPULSE Pulsed Field Ablation System

Objective

The primary objective of the FARA-Freedom Study was to provide ongoing post-market demonstration of the safety and performance of the FARAPULSE Pulsed Field Ablation System in the treatment of patients with Paroxysmal Atrial Fibrillation (PAF), when used commercially in Europe.

Design, Scope and Methods

The FARA-Freedom Study was a prospective, open label, post market study conducted at 14 centers in Europe. All treated subjects were followed for 360 days post-ablation with weekly event monitoring beginning on Day 90, and

72-hour Holter monitoring at Days 180 and 360. Clinical follow-up at Days 7, 30, 90, 180 and 360 were performed to determine any occurrence of adverse events or arrhythmia recurrence. The interim study analysis results from this study were provided as supplementary clinical evidence to support the safety and effectiveness of the FARAPULSE PFA System using statistical analyses that are identical or analogous to the methods used for the ADVENT Trial.

Endpoints

The primary safety endpoint was a Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device or procedure-related SAEs as adjudicated by the CEC.

Acute Primary safety endpoints were the following with an onset date within 7 days of the Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation
- Pericarditis
- Pulmonary edema
- Vascular access complications
- Heart block
- Gastric motility/pyloric spasm disorders

Late onset primary safety endpoints were the following with an onset date any time through the completion of 12-month follow-up visit:

- Pulmonary Vein Stenosis (PVS)
- Atrio-esophageal fistula

The safety hypotheses are as follows:

$H_0: Q_T \geq PG_{saf}$

$H_A: Q_T < PG_{saf}$,

where QT is the probability of an MITT subject experiencing one or more CSE, and PGsaf is a performance goal of 0.14. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the upper bound of a 95% central Bayesian credible interval (BCI) being less than PGsaf. The parameter QT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of QT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis, using the same approach that is used in the ADVENT Statistical Analysis Plan.

The primary performance endpoint was Treatment Success in MITT subjects through the Month 12 Assessment defined as:

1. Acute Procedural Success AND
2. Chronic Success, defined as freedom from:
    a. At the Index / Rescheduled Index Procedure: Use of a non-PFA treatment modality for PVI
    b. After the Blanking Period, occurrence of any Detectable AF, AFL or AT excluding CTI-dependent AFL confirmed by EP study, any cardioversion for AF, AFL or AT (excluding for CTI-dependent AFL), Use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT
    c. At any time re-ablation for AF, AFL or AT (other than for CTI-dependent AFL) or use of amiodarone, except intra-procedurally to control an arrhythmia.

The performance hypotheses are as follows:

$H_0: P_T \leq PG_{perf}$

$H_A: P_T > PG_{perf}$,

where PT is the probability of a subject being a Treatment Success at 12 Months, and PGperf is a pre-specified performance goal of 0.50. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the lower bound of a 95% central Bayesian credible interval (BCI) being greater than PGperf. PT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of PT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis.

Subject Accountability

All subjects who signed and dated the Informed Consent Form were considered enrolled in the study.

Intent-to-Treat (ITT) Subjects are subjects who met all the following criteria:

- The subject signed the informed consent document
- The subject was determined by the site to meet all pre-procedural study eligibility criteria
- The subject began the Index Procedure

Modified Intent-to-Treat (MITT) Subjects are ITT Subjects who received any energy delivery for PVI with the FARAPULSE Pulsed Field Ablation System at an Index / Rescheduled Index Procedure.

A total of 185 subjects were enrolled in the study and a total of 180 subjects were treated with the FARAPULSE Pulsed Field Ablation System. The ITT, MITT, and Safety analysis sets consist of the same population (N=180), as all subjects received energy delivery for PVI with the FARAPULSE Pulsed Field Ablation System.

Study Population Demographics, Baseline Characteristics, and Visit Compliance

The demographics of the study population represented a typical PAF catheter ablation patient. Mean age was 62.3 years and 61.1% were male. Mean LVEF was 60.8 % and mean LAD was 4.0 cm. The mean CHA2DS2-VASc Score was 1.8. Palpitations were the most prevalent baseline AF symptom reported in subjects (76.7%) with a mean frequency of 11.0 palpitations over the previous two-month period. The most common comorbidities were hypertension (55%) and dyslipidemia (38.9%).

Study subjects were scheduled for assessment at Baseline, Index Procedure, Pre-Discharge, Days 7, 30, 60, 90, 180 and Day 360. Visit compliance for these study assessments was high at 99.3% overall, and 96.8% of visits conducted within protocol window. The overall rhythm monitoring weekly compliance was high, with 89.1% of monitored weeks resulting in an evaluable rhythm monitoring record for study subjects .

Procedural Durations

Ablations were performed using the FARAPULSE Pulsed Field Ablation System, with either the 31 mm or 35 mm FARAWAVE Pulsed Field Ablation Catheter, using a recommended minimum of 8 applications in each PV at between 1.8 and 2.0 kilovolts (kV).

The duration of clinically relevant portions of each Index Procedure were recorded and compared descriptively.

Overall procedure time averaged 72 minutes; this is inclusive of the protocol-required 20-minute wait time following the last ablation. Longer procedure durations occurred in subjects that had an acute reconnection of the PV requiring a touch up to be performed thereby adding an additional 20-minute wait period as specified per protocol. Total ablation time averaged 17.8 minutes. Mean LA dwell time was 40.9 minutes, which is inclusive of the 20-minute wait time post-ablation.

Results

<u>Primary Safety Endpoint</u>

Two (2) subjects experienced one or more CSE events therefore the estimated incidence through 12 months is 1.4%, and the upper bound of the 95% BCI is 3.7%. The posterior probability that the incidence is less than the pre-specified performance goal of 14% is >0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion.

Table 11. Summary of Subjects with one or more CSE

Safety Subjects with One or More CSE Events by Event Type	Number of Subjects % (n / N) N=180
Any CSE Event	1.1 (2/180)
Death	0.0 (0/180)
Myocardial infarction	0.0 (0/180)
Persistent phrenic nerve palsy	0.0 (0/180)
Stroke	0.0 (0/180)
TIA	0.6 (1/180)
Peripheral organ thromboembolism	0.0 (0/180)
Cardiac tamponade or perforation	0.6 (1/180)
Pericarditis	0.0 (0/180)
Pulmonary edema	0.0 (0/180)
Vascular access complication	0.0 (0/180)
Heart block	0.0 (0/180)
Gastric motility/pyloric spasm	0.0 (0/180)
Pulmonary vein stenosis	0.0 (0/180)
Atrio-esophageal fistula	0.0 (0/180)

Note 1: n = number of subjects with event, N = number of safety subjects.

Abbreviations: CSE = Composite Safety Endpoint, TIA = transient ischemic attack

Additional Safety Information

Overall, 137 adverse events were experienced in 69 subjects. There were no incidences of persistent phrenic nerve palsy, no occurrences of pulmonary vein stenosis, and no atrio-esophageal fistulas occurring at any time during study follow-up.

There were no Unanticipated Adverse Device Effects (UADEs) in the FARA-Freedom Study.

Table 12. Summary of Adverse Events

Adverse Events Categories- MITT	All Subjects (N=180) n (%) e[1]
Any adverse event	69 (38%) 137
Any SAE	20 (11%) 31
Any device-related AE	6 (3%) 6
Any procedure-related AE	26 (14%) 31
Any device-related SAE	1 (1%) 1
Any procedure-related SAE	7 (4%) 9

Note 1: N = number of MITT in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Serious Adverse Events

The following table summarizes the incidence of all SAEs by AE Category. There were 7 device- or procedure-related SAEs reported in 9 subjects. One (1) event of TIA was assessed by the CEC as possibly related to the device and probably related to the procedure. All other events were classified as procedure related only by the CEC. All of these SAEs were determined to be resolved by the without reported sequelae.

Table 13. Related Serious Adverse Events by Category – MITT Subjects

Procedure- or Device-Related Serious Adverse Events	All Subjects (N=180) n (%) e[1]
Procedure- or Device-Related Serious Adverse Events	7 (4%) 9
Atrial flutter	1 (1%) 2

Procedure- or Device-Related Serious Adverse Events	All Subjects (N=180) n (%) e[1]
Procedure related Abnormal labs	2 (1%) 2
Angina/Chest Pain - Post EP procedure	1 (1%) 1
Atrial tachycardia/Other SVT	1 (1%) 1
Myocardial Perforation with Tamponade	1 (1%) 1
Pseudoaneurysm	1 (1%) 1
TIA	1 (1%) 1

Note 1: N = number of MITT subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Primary Performance Endpoint

The estimated probability of MITT subjects experiencing Treatment Success was 66.3% (lower bound of the 95% BCI is 59.1, upper bound is 73.1). The posterior probability that this success rate exceeds the pre-specified performance goal of 50% is > 0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion.

Table 14. Primary Performance Endpoint – MITT Subjects

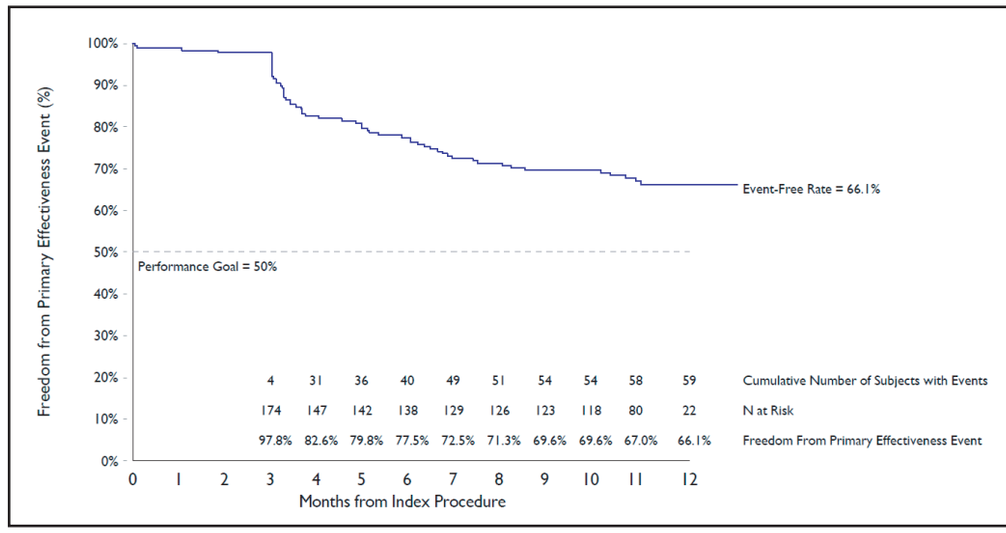
Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] N = 180	Incidence (%)	95% BCI	Posterior Probability of Treatment Success Proportion > 50%
90 [31]	66.3	[59.1, 73.1]	>0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

An additional analysis of the primary performance endpoint was performed using the Kaplan-Meier method to include incomplete subject data. This is a different statistical technique applied to a slightly different definition of the endpoint (time to failure rather than Treatment Success at the 12-month visit), but the Kaplan-Meier estimate of 66.1% at 360 days agrees closely with the 66.3% estimate produced by the pre-specified Bayesian statistical model. These data are displayed in the following graph.

Figure 3. Survival Analysis, Primary Performance Endpoint



The mode of the earliest failure of the primary effectiveness endpoint for each MITT subject is detailed in the following table.

Table 15. Earliest Primary Effectiveness Failure Modes – MITT Subjects

First Primary Effectiveness Failure Mode	Number of Subjects with Event N = 180	Estimated Incidence (%)[1]	95% BCI[1]
Any Primary Effectiveness Failure Mode[2]	59	33.7	[26.9, 40.9]
Acute Procedural failure	0	0.3	[0.0, 1.4]
PVI performed with non-PFA device	0	0.3	[0.0, 1.4]
Post-blanking Detectable AF/AFL/AT/SVT	41	23.6	[17.6, 30.2]
Post-blanking Detectable AF	31	17.9	[12.6, 23.9]
Post-blanking Detectable AFL	0	0.3	[0.0, 1.6]
Post-blanking Detectable AT	8	4.8	[2.2, 8.4]
Post-blanking Detectable SVT	2	1.5	[0.3, 3.9]
Post-blanking cardioversion for AF/AFL/AT	0	0.3	[0.0, 1.6]
Post-blanking use of Type I/III AAD	12	7.1	[3.8, 11.3]
Any re-ablation for AF/AFL/AT	3	2.0	[0.5, 4.6]
Any non-procedural use of amiodarone	3	2.0	[0.5, 4.5]

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)

Note 1: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

Note 2: Each subject has only one earliest primary effectiveness failure mode.

Additional Performance Information

Acute Procedure Success was defined as the proportion of all attempted PVs isolated using the FARAWAVE Pulsed Field Ablation Catheter during the Index procedure, as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing. All ablated PVs achieved Acute Vein success (100%).

Study Conclusion

The primary safety and performance endpoint analysis from the European FARA-Freedom PMCF Study provides supplemental evidence supporting the safety and performance of the FARAPULSE PFA System in the treatment of patients with PAF.

ADVANTAGE AF Clinical Study Phase 1

Study Title	A Prospective Single Arm Open Label Study of the FARAPULSE Pulsed Field Ablation System in Subjects with Persistent Atrial Fibrillation
Number of Centers	43 sites in the North America and Europe
Number of Subjects	355 enrollments, including 79-roll-in subjects, 16 Consent Ineligible/ Intent, and 260 non-roll-in subjects treated with the FARAPULSE Pulsed Field Ablation System.

Objective

The objective of the ADVANTAGE AF Study was to establish the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System (FARAPULSE PFA System) for the treatment of drug refractory, symptomatic persistent atrial fibrillation (PersAF).

Design, Scope, and Methods

The ADVANTAGE AF Study Phase 1 was a prospective, single arm, open label, multi-center IDE pivotal study conducted at 43 sites in the United States (39), Canada (2), and Europe (2). A total of 355 subjects were enrolled in the study and a total of 339 were treated with the FARAPULSE Pulsed Field Ablation System. All subjects who met eligibility criteria, signed the informed consent, and underwent the Index Procedure were followed post-ablation for twelve (12) months with twice per month event monitoring plus symptom-driven event monitoring beginning on Day 90, a 24 Hour Holter monitor at Day 180 and Day 360 and clinical follow ups at Day 7, Day 30, Day 90, Day 180 and Day 360 to determine any occurrence of adverse events or arrhythmia recurrence.

Endpoints

The primary safety endpoint (PSE) was the proportion of Treatment Subjects and Attempt Subjects with one or more of the following device or procedure-related Composite Serious Adverse Events (CSAEs) following the Index Procedure / Rescheduled Index Procedure or the Re-Ablation Procedure within the Blanking Period, with an Onset Date following the procedure as specified in the table below.

Table 16. CSAEs Following Index Procedure/Rescheduled Index Procedure or Re-Ablation Procedure Within 3-Month Blanking Period

Composite Serious Adverse Events	Onset Date
• Death • Myocardial infarction • Stroke • TIA • Peripheral or organ thromboembolism • Pulmonary edema • Unresolved phrenic nerve palsy/paresis • Vascular access complications • Heart block • Gastric motility/pyloric spasm disorders	Day 0 – Day 7
• Cardiac tamponade/perforation • Pericarditis	Day 0 – Day 30
• PV stenosis • Atrio-esophageal fistula	Day 0 – Day 360 Assessment

The primary effectiveness endpoint (PEE) was the proportion of Treatment Subjects with Treatment Success through the Day 360 Assessment.

Treatment Success was defined as:

1. Persistent AF Acute Procedural Success AND
2. Persistent AF Chronic Success, defined as freedom from the following after the 3-month Blanking Period (excluding documented CTI-dependent atrial flutter):
   - **i. Arrhythmia**: Occurrence of any Detectable AF, AFL or AT
   - **ii. Re-ablation:** Any re-ablation for AF, AFL or AT
   - **iii. Cardioversion:** Any electrical cardioversion for AF, AFL or AT
   - **iv. AAD Use:** Use of a Non-Failed Class I / III AAD or amiodarone

Subject Accountability

All subjects who signed and dated the informed consent were considered enrolled in the study and classified as either Roll-In or Non-Roll-In subjects.

Roll-In Subject - The first subject enrolled by each Investigator at each site was treated with the FARAPULSE Pulsed Ablation System as part of Investigator preparation and was enrolled into the study as a Roll-In Subject.

Non Roll-In Subject - After the Roll-in subject criteria was satisfied for the treating physician, Non Roll-In subjects could be enrolled.

Roll-in and Non Roll-In subjects were further classified as Consent Ineligible, Intent, Attempt, or Treatment.

- **Consent Ineligible** – any subject who signed informed consent but was found ultimately not to meet eligibility criteria
- **Intent** – Intent subjects included the following type of subjects
  - Any subject who signed informed consent, met eligibility criteria, but did not have any study investigational devices inserted into the body
  - Any subject that was enrolled in the study but did not undergo the Index Procedure within 30 days from the Consent Date or a Rescheduled Index Procedure within 45 days of the Index Procedure. These subjects were withdrawn from the study as of the end of the above disqualifying interval.
- **Attempt** – any subject who signed informed consent, met eligibility criteria, and had an investigational

device inserted into the body but did not receive any pulsed field ablation application

- **Treatment** – any subject who signed informed consent, met eligibility criteria, had an investigational device inserted into the body and received at least one pulsed field ablation application

A total of 355 subjects (79 Roll-In, 10 Consent Ineligible, 6 Intent and 260 Non-Roll-In Treatment subjects) were enrolled in the ADVANTAGE AF Study Phase 1 across 43 investigational sites in the United States, Canada, and Europe. There were 79 Roll-In subjects and 260 Non Roll-in subjects that received treatment with the FARAPULSE system. Primary analyses were performed on the 260 Non Roll-In Treatment subjects who will henceforth be referred to as "Treatment subjects".

Study Population Demographics, Baseline Parameters, and Visit Compliance

Key baseline demographics and clinical characteristics of the Treatment subjects are presented in Table 17 and 18 below. The mean age of Treatment subjects in the ADVANTAGE AF Study Phase 1 was 66.2 ± 9.3 years. The majority of the subjects were male (69.2%) and all subjects met the eligibility criteria of having a persistent AF diagnosis. As expected with a persistent AF population, the majority of subjects (185, 71.2%) had previously undergone a cardioversion procedure.

Table 17. Baseline Demographics

Characteristic	Measurement	Subjects (N=260)
Age (years)	n Mean ± SD (Median) Range	260 66.2 ±9.3 (67.5) (35.0 - 87.0)
Sex	Male	180 (69.2%)
	Female	80 (30.8%)
Ethnicity	Not disclosed	45 (17.3%)
	Not Hispanic or Latino	211 (81.2%)
	Hispanic or Latino	4 (1.5%)
Race[1]	Not disclosed	45 (17.3%)
	White	209 (80.4%)
	Black or African American	4 (1.5%)
	Asian	3 (1.2%)

n is number of subjects; SD is standard deviation;
Categorical results are number of subjects (% of total subjects [N] with non-missing values).
[1]Subjects may contribute to more than one category

Table 18. Baseline Characteristics

Characteristic	Measurement	Subjects (N=260)
BMI (kg/m2)	n Mean ± SD (Median) Range	260 30.4 ± 5.3 (29.8) (15.0 - 41.9)
LVEF (%)	n Mean ± SD (Median) Range	259 57.2 ± 6.9 (58.0) (40.0 - 73.0)
LA Diameter (cm)	n Mean ± SD (Median) Range	228 4.3 ± 0.6 (4.3) (2.5 - 5.4)
LA Volume (mL)	n Mean ± SD (Median) Range	32 65.1 ± 24.6 (70.0) (25.0 - 100.0)
Cardiac Procedure History	Prior cardiac ablation	9 (3.5%)
	Coronary Artery Bypass Grafting (CABG)	9 (3.5%)
	Valvular Surgery	0 (0.0%)

Characteristic	Measurement	Subjects (N=260)
Cerebrovascular Disease History	Cerebral Vascular Accident (CVA)/Stroke	14 (5.4%)
	Transient Ischemic Attack (TIA)	6 (2.3%)
Cardiovascular Disease History	Hypertension	165 (63.5%)
	Valvular Heart Disease	20 (7.7%)
	Peripheral Vascular Disease	10 (3.8%)
	Coronary Artery Disease	61 (23.5%)
	Acute Myocardial Infarction (MI)	15 (5.8%)
NYHA Functional Class	No Heart Failure	173 (66.8%)
	Class I	42 (16.2%)
	Class II	44 (17.0%)
	Class III	0 (0.0%)
	Class IV	0 (0.0%)
CHA2DS2-VASc score	0	31 (11.9%)
	1	47 (18.1%)
	2	59 (22.7%)
	3	64 (24.6%)
	4	43 (16.5%)
	5	12 (4.6%)
	6	4 (1.5%)
Comorbidities	Diabetes	44 (16.9%)
	Dyslipidemia	117 (45.0%)
	Obstructive Sleep Apnea	72 (27.7%)
	COPD	17(6.5%)
	Renal Dysfunction/ Failure	7 (2.7%)
History of Refractory or Non-tolerant AADs	Amiodarone	80 (30.8%)
	Dofetilide	15 (5.8%)
	Dronedarone	31 (11.9%)
	Sotalol	47 (18.1%)
	Flecainide	89 (34.2%)
	Propafenone	15 (5.8%)
Anticoagulants at Baseline	DOAC	257 (98.8%)
	VKA	5 (1.9%)

Characteristic	Measurement	Subjects (N=260)
Cardiac Arrhythmia History	History of Atrial Fibrillation[1]	260 (100.0%)
	Paroxysmal Atrial Fibrillation	82 (31.5%)
	Persistent Atrial Fibrillation	260 (100.0%)
	Long Standing Persistent Atrial Fibrillation	0 (0.0%)
	Years since first AF diagnosis	
	n Median (IQR) Range	260 1 (0 - 4) (0 - 41)
	Atrial Flutter	63 (24.2%)
	CTI dependent flutter	41 (15.8%)
	Atypical flutter	8 (3.1%)
	Unknown	10 (3.8%)
	Other flutter[2]	4 (1.5%)
	Atrioventricular Block/Conduction Disease	32 (12.3%)
	1st degree AV block	32 (12.3%)
	2nd degree AV block	0 (0.0%)
	3rd degree AV block	0 (0.0%)
	Sinus Bradycardia	96 (36.9%)
	Sinus Tachycardia	8 (3.1%)
	Ventricular Tachycardia	4 (1.5%)
	Premature Ventricular Contractions	4 (1.5%)
	Right Bundle Branch Block	3 (1.2%)
	Sinus Node Dysfunction	2 (0.8%)
	Junctional Arrhythmia	1 (0.4%)
	Other Cardiac Arrhythmia[3]	9 (3.5%)
Cardioversion History	None	75 (28.8%)
	n Median (IQR) Range	185 1 (1 - 2) (1 - 6)
Baseline 12-lead ECG Rhythm	Atrial Fibrillation	150 (57.7%)
	Sinus Rhythm	88 (33.8%)
	Sinus Bradycardia	14 (5.4%)
	Atrial Flutter	8 (3.1%)

n is number of subjects; IQR is inter-quartile range;
Categorical results are number of subjects (% of total subjects [N] with non-missing values).
[1]Subjects may contribute to more than one category
[2]Other atrial flutter types included: PV flutter, paroxysmal a-flutter, 1:1 AV conduction at 140 bpm, variable with AV block
[3]Other cardiac arrhythmia history included: Ibbb; one run of VT lasting 4 beats; SVT and AT; AT, SVT, and atrial bradycardia; ectopic atrial rhythm; ventricular extrasystole; bidirectional block and a left anterior hemi-block with a RBBB; Ibbb; possible ectopic atrial rhythm

Follow-up visit compliance (pre-discharge, Day 7, Day 30, Day 90, Day 180 and Day 360) was high with an overall compliance rate of 99.4%. Post-ablation rhythm monitoring included symptomatic and twice per month event monitor transmissions during the evaluation period, 12-Lead ECGs at Day 90 and Day 360, and 24-Hour Holter monitors at Day 180 and Day 360. The overall rhythm monitoring compliance for event monitor transmission, 12-lead ECG, and 24-hour Holter was 73.2%, 94.6%, and 92.2%, respectively.

Procedural Characteristics

The duration of clinically relevant portions of each Index Procedure were recorded descriptively: procedure time (103.0 ± 34.8 minutes), LA dwell time (58.5 ± 19.9 minutes), PVI ablation time (26.8 ± 15.0 minutes), PWI ablation time (18.4 ±

15.0 minutes), and other ablation time (22.6 ± 18.0 minutes). The total procedure time was inclusive of the 20-minute waiting period required per protocol prior to assessing for PV entrance block and inclusive of all ablations, including ablation to the PVs, PW, CTI, and additional lesion sets. Fluoroscopy time was 19.5 ± 13.1 minutes. An anchoring technique of placing a wire within an adjacent PV while using sheath support to position the FARAWAVE PFA Catheter superiorly to ablate antral/ superiorly during posterior wall ablation was optional and utilized in 71.8% of procedures. Additional procedure characteristics can be found in table 19.

Table 19. Additional Index Procedure Characteristics

Characteristic	Measurement	Index Procedures (N=260)
Method of Anesthesia	General anesthesia	226 (86.9%)
	Conscious sedation/Monitored Anesthesia Care (MAC)	34 (13.1%)
Screening for LA Thrombus Performed	Yes	260 (100.0%)
LA Thrombus Identified	Yes	0 (0.0%)
ACT levels Maintained >300	Yes	256 (98.5%)
Other Ablations Using a Commercially Available RF Catheter	Treatment-emergent left AFL	8 (3.1%)
	Treatment-emergent AT	1 (0.4%)
	CTI-dependent AFL	50 (19.2%)
IV fluids administered (mL)	Yes	260 (100.0%)
Volume of IV fluids administered (mL)[1]	Mean ± SD (Median) Range	932.5 ± 532.8 (850.0) (11.0 - 3700.0)
Contrast dye injected	Yes	10 (3.8%)
Volume of contrast dye injected (mL)	Mean ± SD (Median) Range	25.4 ± 21.3 (23.0) (5.0 - 65.0)
PFA Applications	PVI	45.1 ± 9.3
	PWI	32.0 ± 12.7
Same Day Discharge	Same Day	141 (54.2%)

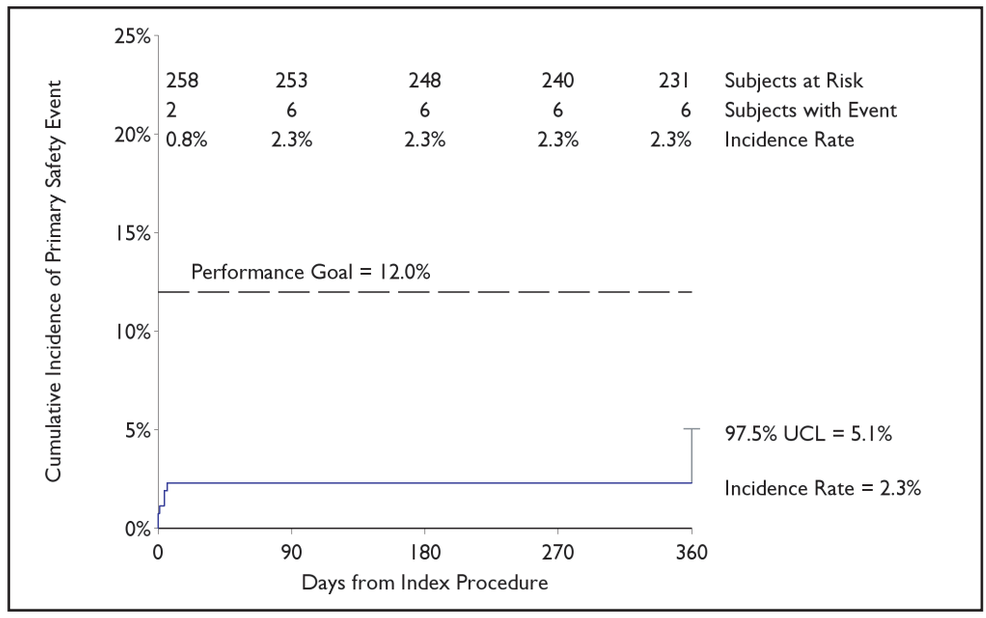
[1]3 procedures with unknown IV fluid volume

Results

Primary Safety Endpoint

Out of 260 Treatment subjects, 6 subjects experienced a device- or procedure-related Composite Serious Adverse Event (CSAE) through Day 360 for a cumulative primary safety event incidence rate of 2.3% (Figure 4). The 97.5% one-sided upper confidence limit (UCL) of the cumulative incidence rate was 5.1%, which was lower than the predefined performance goal of 12%. Therefore, the Primary Safety Endpoint was met.

Figure 4. Primary Safety Endpoint Result



The device- or procedure-related CSAEs that occurred following the Index Procedure are summarized in Table 20. Each event was classified by the ADVANTAGE AF Clinical Events Committee (CEC) following pre-defined CSAE definitions.

Table 20. Primary Safety Events

Primary Safety Event Type	Subjects with an Event[1] (% of Total Subjects) (N=260)
Myocardial Infarction	1 (0.4%)
Pericarditis	1 (0.4%)
Pulmonary edema	4 (1.5%)

[1]Subjects may experience multiple Primary Safety Endpoint event types.

Additional Safety Information

Related Adverse Events

There were a total of 55 serious adverse events reported in 44 (16.9%) Treatment subjects. A total of 26 (47.3%) serious adverse events were adjudicated by the CEC as not device or procedure related. The remaining 29 events were adjudicated as serious and procedure related with a subset of 5 events also adjudicated as device related (Tables 21 and 22). The device related serious adverse events included one (1) oozing/ bleeding event, adjudicated by the CEC as related to the FARADRIVE Steerable Sheath, 3 arrhythmia events, adjudicated as unrelated to the PFA catheter and sheath but related to another component of the FARAPULSE PFA system, and one (1) hemolysis event, further described below.

A total of 29 procedure related serious adverse events occurred in 22 (8.5%) Treatment subjects. The largest category of procedure related serious adverse event was genitourinary/renal with 7 events in 6 Treatment subjects. Details of the 7 serious genitourinary/renal events are as follows: 4 urinary retention events, 2 hematuria events, and one (1) acute kidney injury. This acute kidney injury was attributed to dehydration by the investigator but no hemolysis biomarkers (e.g., haptoglobin and plasma free hemoglobin) were tested. This procedure related serious adverse event resolved with intravenous fluid hydration.

Two Treatment subjects had procedure-related acute kidney injury, resulting in a rate of procedure-related acute kidney injury of 0.8% in the Non Roll-In Treatment subjects. One acute kidney injury was considered to be secondary to dehydration as discussed above. The other acute kidney injury occurred secondary to intravascular hemolysis (laboratory confirmed) and was adjudicated by the CEC as a procedure-related serious adverse event. This subject received 93 total PFA applications and sustained acute kidney injury (with elevation of creatinine from 1.2 to 2.3 mg/ dL) before normalizing with conservative management.

There was one (1) acute coronary syndrome requiring percutaneous coronary intervention and stent placement reported in a Treatment subject who suffered an acute myocardial infarction during the index procedure. Coronary

angioplasty report noted that the etiology of the acute myocardial infarction was unclear but there was presence of clot and vasospasm in otherwise normal arteries. The adverse event was adjudicated by the CEC as an acute myocardial infarction, a primary safety event, related to the index procedure but unable to determine its relationship to the study catheter, sheath, or any other component of the ablation system.

There was one peripheral embolic event reported in a Treatment subject (0.4%). It was a renal infarction that occurred three (3) weeks post procedure in a subject who that received 60 PFA applications during the index procedure. The CEC adjudicated the event as procedure-related serious adverse event, not related to the study catheter or sheath, but unable to determine if it was related to any other component of the ablation system.

Table 21. Procedure-related Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Total	22 (8.5%)	29
Procedure related Genitourinary/Renal	6 (2.3%)	7
Procedure related Anesthesia/Sedation	1 (0.4%)	1
Oozing/Bleeding	2 (0.8%)	2
Atrial Fibrillation (AF)	4 (1.5%)	4
Atrial tachycardia/Other SVT (e.g. AVRT, AVNRT, EAT)	2 (0.8%)	2
Procedure related Heart Failure	3 (1.2%)	3
Procedure related Pulmonary (including cough, hemoptysis)	2 (0.8%)	2
Fluid volume overload	1 (0.4%)	1
Hemolysis (Laboratory confirmed*)	1 (0.4%)	1
Procedure related Hypotension	1 (0.4%)	1
Coronary artery injury/Spasm	1 (0.4%)	1
Genitourinary	1 (0.4%)	1
Multiple Heart Failure symptoms	1 (0.4%)	1
Post procedure infection/sepsis	1 (0.4%)	1
Renal Infarction	1 (0.4%)	1

*Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

Table 22. Device-related* Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Total	5 (1.9%)	5
Atrial tachycardia/Other SVT (e.g. AVRT, AVNRT, EAT)	2 (0.8%)	2
Atrial Fibrillation (AF)	1 (0.4%)	1
Hemolysis (Laboratory confirmed**)	1 (0.4%)	1
Oozing/Bleeding	1 (0.4%)	1

*All device-related events were also classified as procedure-related. Events appear in both Table 21 and 22.

**Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

In addition, there were 75 procedure related non-serious adverse events reported in 50 (19.2%) subjects. These included 10 (3.8%) procedure related genitourinary/ renal events reported in 10 subjects (3.5%), which consisted of one (1)a urinary tract infection, 2 hematuria, and 7 urinary retention/ decreased urine output. There was also one (1) non-serious procedure related adverse event reported as for laboratory confirmed hemolysis in a subject who that presented with choluria; and there was one (1) temporary phrenic nerve injury reported in a Treatment subject (0.4%), as seen in Table 23.

Table 23. Select Procedure-related Non-Serious Adverse Events in Non Roll-In Treatment Subjects

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%) (N=260)**	**Events**
Procedure related Genitourinary/Renal	10 (3.8%)	10
Hemolysis (Laboratory confirmed*)	1 (0.4%)	1
Phrenic nerve injury temporary	1 (0.4%)	1

*Decreased haptoglobin and/or combination of positive hemoglobin in urine, elevated LDH, and/or elevated indirect bilirubin

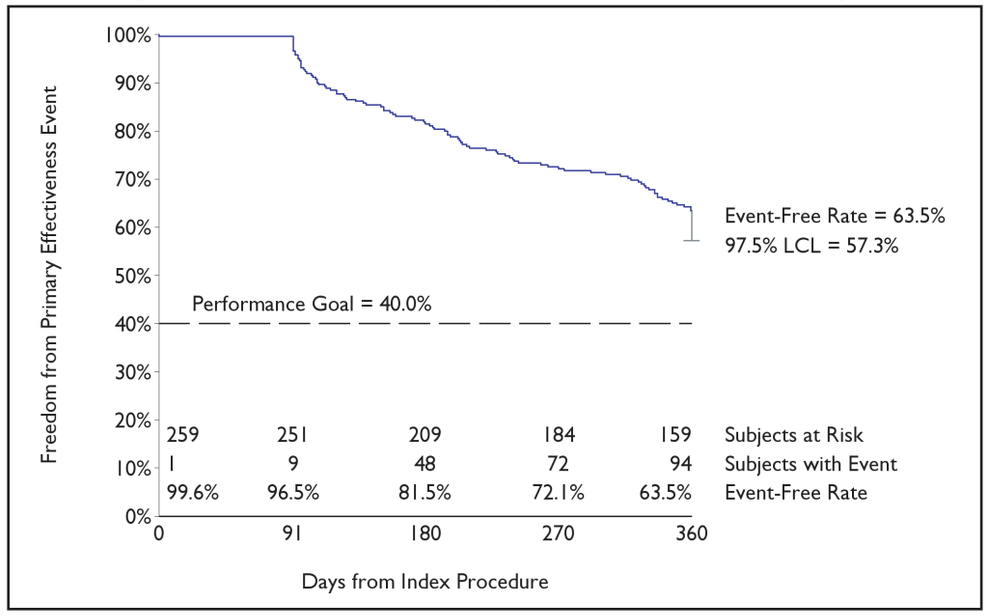
Primary Effectiveness Endpoint

Of the 260 Treatment subjects that underwent an Index Ablation Procedure, 259 (99.6%) reported acute procedural success. One subject was classified as an acute procedural failure due to repeated console errors which required the operator to switch to an RF catheter to complete the procedure. All subjects, including the subject whose procedure was completed using RF, had PVI and PWI achieved.

The second component of the primary effectiveness endpoint is chronic success. Of the 260 Treatment subjects, 93 (35.8%) subjects experienced at least one mode of chronic treatment failure through 360 days of follow-up.

In total, 94 subjects experienced a primary effectiveness failure event through Day 360 post-Index Procedure resulting in a Treatment Success rate of 63.5% with a one-sided 97.5% lower confidence limit (LCL) of 57.3% (Figure 5). Since the LCL was greater than the pre-specified performance goal of 40%, the Primary Effectiveness Endpoint was met.

Figure 5. Freedom from Primary Effectiveness Failure at Day 360



The first and subsequent primary effectiveness failure events are summarized in Table 23. Each subject was considered an endpoint failure at the time of the first event. Subsequent events are presented for completeness. The most common reason for treatment failure was documented AF/AT/AFL post-blanking period and the majority of the documented arrhythmia recurrences was AF.

Table 24. Primary Effectiveness Failure Events

	Subjects with an Event (% of Total Subjects) (N = 260)	
Primary Effectiveness Event Type	**First Failure Event**	**All Failure Events[1]**
Acute procedural failure	1 (0.4%)	1 (0.4%)
Use of a non-study ablation catheter	1 (0.4%)	1 (0.4%)
Documented AF/AT/AFL post-blanking period	79 (30.4%)	88 (33.8%)
≥30 seconds recorded on Event Monitor	65 (25.0%)	76 (29.2%)

	Subjects with an Event (% of Total Subjects) (N = 260)	
Primary Effectiveness Event Type	**First Failure Event**	**All Failure Events[1]**
≥30 seconds recorded on Holter Monitor	8 (3.1%)	33 (12.7%)
≥10 seconds recorded on 12-Lead ECG	6 (2.3%)	26 (10.0%)
AAD use post-blanking period	11 (4.2%)	19 (7.3%)
Use of a non-failed Class I/III AAD post-blanking period	7 (2.7%)	12 (4.6%)
Amiodarone use post-blanking period	4 (1.5%)	7 (2.7%)
Cardioversion for AF/AT/AFL post-blanking period	2 (0.8%)	17 (6.5%)
Re-ablation for AF/AT/AFL post-blanking period	1 (0.4%)	12 (4.6%)

N is total Treatment subjects
[1]Subjects may have multiple failure event types.

Additional Effectiveness Analyses

1. Single Procedure Treatment Success

Single Procedure Treatment Success was defined as freedom from Primary Effectiveness Endpoint failure without a re-ablation procedure for AF, AFL, or AT. There were two Treatment subjects who had re-ablations using the FARAWAVE Catheter during the blanking period and therefore contributed additional failures for the Single Procedure Treatment Success endpoint. However, both subjects experienced atrial arrhythmia recurrence following the blanking period and were therefore already considered effectiveness failures in the Primary Effectiveness Endpoint. Thus, the proportion of subjects with Single Procedure Treatment Success was identical to the proportion of subjects with Primary Effectiveness Endpoint success, 63.8% (166/260) in the Non Roll-In Treatment subjects.

2. Off Drug Treatment Success

Off Drug Treatment Success was defined as freedom from Primary Effectiveness Endpoint failure without the use of a Class I or III AAD after the blanking period, including the use of a failed dose. The Off Drug Treatment Success rate was 56.9% (148/260) in the Non Roll-In Treatment subjects.

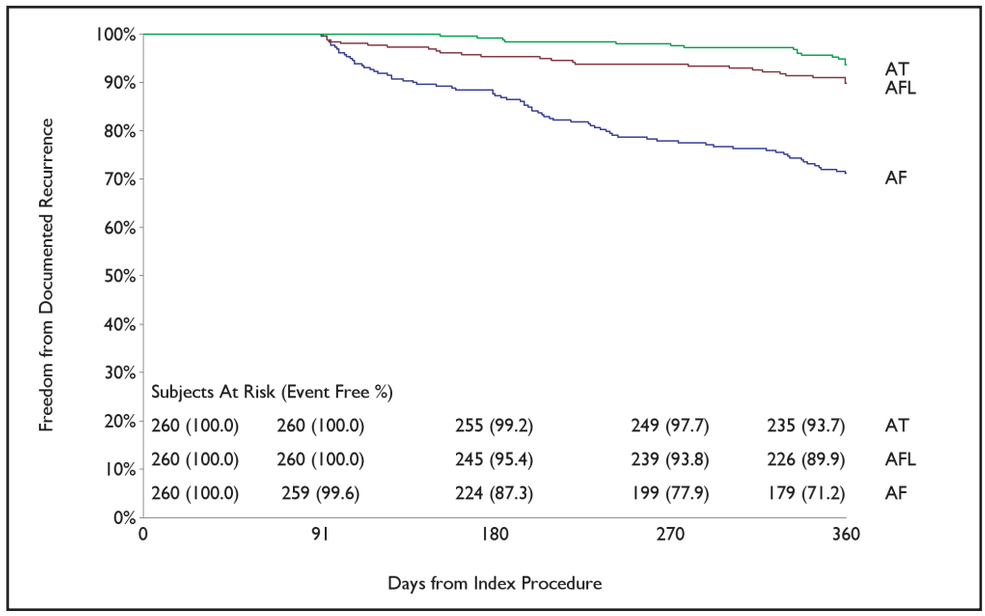
3. Re-Ablation Rate

The Re-Ablation Rate was defined as the proportion of subjects who received one or more re- ablation for AF, AFL, or AT during study follow-up. Among the 260 Non Roll-In Treatment subjects, 14 subjects (5.4%) had one or more repeat ablations during follow-up (two had repeat ablation during the blanking period and 14 had repeat ablation following the blanking period).

4. Type of Recurrence

Of the 260 Treatment subjects, 88 (33.8%) had documented AF, AFL, or AT recurrence post-blanking period (Table 21). There were 51 subjects (19.6%) with only AF recurrence, 5 subjects (1.9%) with only AFL recurrence, and 7 subjects (2.7%) with only AT recurrence. The remaining 25 subjects experienced more than one type of atrial arrhythmia recurrence. The rate of freedom from documented recurrence of each arrhythmia type through Day 360 was 71.2% for AF, 89.9% for AFL, and 93.7% for AT (Figure 6).

Figure 6. Freedom from Documented Recurrence by Rhythm

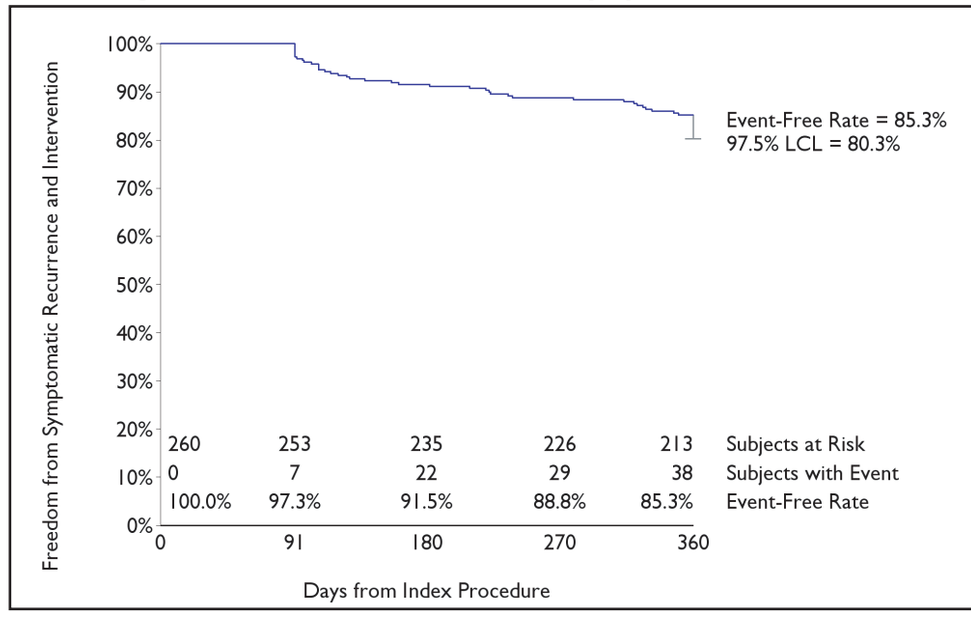


5. Freedom from Documented Symptomatic Recurrence

Given the low rates of re-ablation, AAD use, and cardioversions observed for the Primary Effectiveness Endpoint, a post-hoc analysis was performed to assess the impact of failures due to asymptomatic recurrence only. Subjects who experienced asymptomatic AF, AT, or AFL recurrence meeting the Primary Effectiveness Endpoint definition but had no intervention to treat the recurrence (re-ablation, cardioversion, or prescription of a non-failed Class I/III AAD or amiodarone) and had no reported symptomatic recurrence recorded by event monitor, were considered to have Treatment Success, rather than Treatment Failure in the post-hoc analysis.

The rate of subjects with freedom from symptomatic recurrence or intervention to treat recurrence was 85.3% (Figure 7).

Figure 7. Freedom from Documented Symptomatic Recurrence



Quality of Life Assessments

Subjects were asked to complete Quality of Life (QOL) questionnaires at the Baseline visit, Day 180, and Day 360 Assessments. The EQ-5D-5L was used to measure subjects' health-related quality of life and the Atrial Fibrillation Effect on Quality of Life (AFEQT) was used to evaluate AF-specific quality of life.

All questionnaire scores, including sub-component scores, improved by the Day 180 Assessment with the overall AFEQT score increasing by a median of 24 (IQR: 10-47) points and EQ-5D-5L score increasing by 5 (IQR: 0-15) points. The improved scores were maintained through the Day 360 Assessment.

Study Conclusions

The ADVANTAGE AF Phase 1 Trial results demonstrated the safety and effectiveness of the FARAPULSE Pulsed Field Ablation System for PV isolation and left atrial posterior wall isolation to treat patients with drug refractory symptomatic persistent atrial fibrillation (episode duration less than one year).

HOW SUPPLIED

Device Details

One (1) FARAWAVE Catheter is supplied sterile using an Ethylene Oxide (EO) process.

WARNING: Do not use the device if past the "Use By" date on the device package. Do not use if sterile barrier is damaged or unintentionally opened before use, as use of non-sterile devices may result in patient injury.

Handling and Storage

Handling	Storage
	Store in a cool, dry, dark place.

Handling excursions between -29 °C and 60 °C degrees permitted. Do not use if the FARAWAVE Catheter is exposed to environmental conditions beyond this range.

OPERATIONAL INSTRUCTIONS

Additional Required Items

Intracardiac electrophysiology and cardiac ablation procedures should be performed in a fully equipped clinical electrophysiology lab. In addition to the FARAWAVE Catheter, the following devices and materials are intended to be used:

- FARADRIVE Sheath
- Compatible BSC PFA Generator
- Compatible BSC Recording System Module
- Compatible FARASTAR Catheter Connection Cable
- Standard commercially available 0.035 in (0.89 mm) guidewires
- Irrigation Tubing Set

Optional Additional Equipment

- Compatible Mapping System, software, and accessories
- Compatible BSC Mapping System Module

Preparation

WARNING: Before use, inspect the packaging for any violation of the sterile barrier and inspect the FARAWAVE Catheter for any defects. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire. Do not use potentially contaminated or defective equipment.

WARNING: Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.

Please refer to the operator's manuals and Instructions for Use for the compatible BSC Generator, BSC Mapping System Module, and BSC Recording System Module. Refer to the IFUs for the FARASTAR Catheter Connection Cable, FARADRIVE Sheath and compatible Mapping System for instructions on connecting and operating these systems in conjunction with the FARAWAVE Catheter. Use appropriate accessory cables to connect the catheter to the appropriate accessory equipment.

1. Connect the patient to an ECG recording system to facilitate arrhythmia monitoring per the standard operating procedure of the electrophysiology lab or manufacturer's operator's manual.

Note: This should be done prior to introducing any intracardiac catheters.

2. Open the FARAWAVE Catheter package. Carefully transfer the package contents into the sterile field, maintaining aseptic technique.
3. Connect the FARAWAVE Catheter to a compatible BSC PFA Generator or BSC Mapping System Module using a FARASTAR Catheter Connection Cable, maintaining aseptic technique. Ensure that the cable/catheter connection remains dry throughout the procedure.

Note: If a three-dimensional (3-D) catheter navigation and mapping system is going to be used, please follow the standard operating procedure of the electrophysiology lab or the instructions for use contained in the manufacturer's operator's manual.

4. Turn on the PFA Generator.
5. Obtain femoral vein access under aseptic conditions. Then place an introducer sheath into the vein using a standard percutaneous technique.
6. Obtain left atrial, transseptal access using standard techniques and commercially available equipment.
7. Flush the guidewire lumen and flush port lumen with sterile saline. Connect the flush port to a continuous flush line with pressurized heparinized saline and purge the catheter and tubing of all air bubbles. Ensure all luer fittings are secure.

WARNING: Always verify that the tubing set, catheter, sheath and all connections have been properly cleared of air prior to inserting the catheter into the vasculature. Air entrapped in the tubing, catheter or sheath can cause potential injury or cardiac arrest. The operator is responsible for removing all air from the system.

8. Insert a standard commercially available 0.035" guidewire through the FARAWAVE Catheter until the tip of the wire is aligned with the tip of the catheter.

Caution: Device deployment friction is increased when attempting to deploy the device when the catheter shaft is bent. FARAWAVE Catheter deployment should always occur with the catheter shaft as straight as possible.

Procedure

Standard procedures for electrophysiology studies will be followed.

WARNING: Administer appropriate levels of peri-procedural anticoagulation therapy for patients undergoing left-sided and transseptal cardiac procedures. There is an increased risk of thromboembolism if appropriate anticoagulation levels are not maintained while the transseptal sheath and/or catheter is in the left side of the heart. Administer anticoagulation therapy during and post procedure according to the institution's standards to minimize bleeding and thrombotic complications.

1. Before placing the FARAWAVE Catheter in the sheath, begin continuous irrigation.

WARNING: Always maintain a constant heparinized normal saline infusion to prevent coagulation within the lumen of the catheter that may result in embolism.

2. Compress the splines of the FARAWAVE Catheter for insertion and allow flush to fill the compressed spline array prior to inserting the sheath.

WARNING: Use both fluoroscopy, or other visualization techniques such as echocardiography, and intracardiac electrograms to monitor the advancement and navigation of the catheter to the area of the endocardium under investigation to avoid conduction pathway injury, cardiac perforation or tamponade. Do not rely solely on electromagnetic navigation system display to monitor catheter location.

3. Advance the FARAWAVE Catheter and the guidewire together into the FARADRIVE Sheath taking care to avoid introducing air into the sheath.
4. Once the distal end of the FARAWAVE Catheter has been fully inserted through the valve, slowly aspirate and flush the FARADRIVE Sheath. Refer to the FARADRIVE Sheath IFU for additional instructions on minimizing air ingress.
5. Under standard imaging guidance (e.g. fluoroscopy or echocardiography), track the guidewire to the target pulmonary vein.
6. Advance the FARAWAVE Catheter over the guidewire into the left atrium. Ensure the tip of the catheter is not bent as it advances beyond the sheath. The white proximal marker band on the shaft indicates when the tip of the catheter is entering the deflectable portion of the FARADRIVE Sheath. Once in left atrium, ensure the proximal marker band on the catheter is within or beyond the marker band at the tip of the sheath.

Note: If using the FARAWAVE NAV Catheter, see the Instructions for Use for the compatible BSC Mapping System for additional visualization on the visualization within FARAVIEW.

CAUTION: Avoid allowing the distal end of the catheter to be put into an acute bend, particularly when advancing the catheter beyond the sheath or deploying the catheter. A catheter exchange may be necessary if the catheter deploys improperly.

7. Check that the distal portion of the FARAWAVE Catheter is free to move. Under standard imaging guidance, carefully deploy the distal splines by pressing down the button and sliding it proximally until the splines deploy into the desired shape. Deployment locks when the button is released.

WARNING: Do not deploy the catheter with any portion of the distal splines located within the sheath as it could lead to catheter damage which may result in patient harm.

WARNING: Ensure that the guidewire is properly inserted into the catheter for adequate support during use. Do not attempt to deploy or un-deploy the FARAWAVE Catheter without a guidewire fully inserted, at or past the FARAWAVE Catheter tip. Failure to do so may result in catheter damage and/or patient injury.

8. Position the FARAWAVE Catheter at the ostium of the targeted pulmonary vein. Use both standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the catheter splines and electrodes while obtaining good tissue apposition. Ensure a stable position is achieved before delivering PFA.
9. If applicable, apply sedative bolus per site protocol.
10. Follow the recommended ablation parameters in the table below. (Refer to the PFA Generator IFU for detailed instructions.)

Note: The following table details nominal dose parameters for PV isolation with PFA.

Parameter	Nominal Value (Per PV)
Voltage Amplitude	1.8 kV, 1.9 kV or 2.0 kV
Total PFA Applications	8

Parameter	Nominal Value (Per PV)
PFA Applications in Full Deployment	4
PFA Applications in Partial Deployment	4

Note: Some anatomies may restrict the ability to achieve the partial or full deployment state. In these cases, ablations may be performed in the achievable full or partial deployment state. Incomplete or interrupted deliveries should be repeated.

Note: If spline inversion occurs during manipulation, undeploy the catheter within the body of the left atrium and retract the catheter into the sheath. Rotate the catheter handle 180 degrees while contained within the sheath tip, then insert the cage back into the chamber and attempt deployment again without contacting any anatomical surfaces. If unsuccessful then remove catheter from the patient to inspect the cage and replace it if needed.

11. Deliver ablation from the PFA Generator at the selected output setting.
12. When ablation is complete, verify that the position of the FARAWAVE Catheter has not changed.
13. Deliver an additional application in the same location. Total number of applications at this site is now two (2).
14. Rotate the FARAWAVE Catheter and reposition at the PV ostium using standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the splines and electrodes while obtaining good tissue apposition. The splines should engage the vein in a different position than the previous two ablations. Ensure a stable position is achieved before delivering PFA.
15. Deliver an additional set of two (2) applications. Total number of applications at this site is now four (4).
16. Retract the FARAWAVE Catheter over the guidewire. Change the deployment shape and re-advance to the target ablation site. The splines should engage the vein in a different position than the previous two positions. Ensure a stable position is achieved before delivering PFA.
17. Deliver an additional set of two (2) applications. Total number of applications at this site is now six (6).
18. Rotate the FARAWAVE Catheter and reposition at the PV ostium using standard imaging techniques and intracardiac electrograms to aid in uniform positioning of the splines and electrodes while obtaining good tissue apposition. The splines should engage the vein in a different position than the previous two ablations. Ensure a stable position is achieved before delivering PFA.
19. Deliver an additional set of two (2) applications. Total number of applications at this site is now eight (8).
20. If needed, perform additional ablations.

Note: After energy delivery, the PFA Generator automatically routes the FARAWAVE Catheter electrodes to the EGM Connector. Signals formed from these electrodes can be viewed on the Recording/Mapping System.

WARNING: Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed in the table above, regardless of absence of intracardiac signal.

Note: When using the FARAWAVE Catheter the proximal electrode must remain uncovered for utilizing the full visualization capabilities of the BSC Mapping System.

Catheter Deployment for the Left Atrial Posterior Wall (LAPW) Isolation

1. Check that the distal portion of the FARAWAVE Catheter is free to move. Under standard imaging guidance, carefully deploy the distal splines by pressing down the slider and moving it down the handle until the splines

form into the fully deployed configuration. Lock the deployment by releasing the slider. Refer to Figure 1 for a depiction of full catheter deployment.

2. Retract the FARAWAVE Catheter over the guidewire until the splines contact the mouth of the sheath or shaft electrode is at the mouth of the sheath.
3. Retract the guidewire until it is completely inside the FARAWAVE Catheter's guidewire lumen.

WARNING: When positioning on cardiac structures, the guidewire should be retracted to prevent cardiac perforation or tissue damage.

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4. Advance and/or rotate the FARAWAVE Catheter and the FARADRIVE Sheath together to position it at the desired location on the LAPW. Adjust the positioning of the catheter and sheath as needed to ensure uniform deployment of the catheter splines and electrodes while at the same time obtaining good tissue apposition.
5. Verify the catheter position using standard imaging guidance. Views from other imaging modalities, including electroanatomical mapping system may be used to supplement fluoroscopy.
6. If applicable, apply sedative bolus per site protocol.
7. Deliver ablation from the PFA Generator using a 1.8 kV, 1.9 kV or 2.0 kV setting.
8. When the application is complete, verify that the position of the FARAWAVE Catheter has not changed.
9. Repeat step 7 for a minimum of two applications per catheter site on the LAPW.
10. After completion of the final application at a site, reposition the catheter to the next site on the LAPW, overlapping it with the previous position one-half of the diameter of the fully deployed configuration footprint, and the repeat steps 4 through 9.
11. Continue ablation across the left atrial posterior wall until posterior wall isolation is complete.

Note: After energy delivery, the PFA Generator automatically routes the FARAWAVE Catheter electrodes to the EGM Connector. Signals formed from these electrodes can be viewed on the Recording/Mapping System.

Caution: Intracardiac electrograms recorded from the electrodes on the FARAWAVE Catheter will likely show a significant reduction in amplitude after the first application of PFA. This should not be used as an indication that no further ablation is necessary. The nominal dose of PFA should be delivered in accordance with the parameters listed above, regardless of absence of intracardiac signal.

Note: When using the FARAWAVE Catheter the proximal electrode must remain uncovered for utilizing the full visualization capabilities of the BSC Mapping System.

Note: An optional anchoring technique was used to perform PW ablation in 71.8% of procedures in the ADVANTAGE AF Phase 1 clinical study. To perform this technique, place the wire in the adjacent PV to anchor the guidewire. Then use the sheath to position the catheter to the location of intended antral ablation.

End of Procedure

1. Under standard imaging guidance (e.g. fluoroscopy or echocardiography), track the guidewire to any pulmonary vein.
2. Carefully un-deploy the FARAWAVE Catheter and retract the catheter over the guidewire until it is completely inside the FARADRIVE Sheath.

WARNING: The FARAWAVE Catheter tip and guidewire move forward during device undeployment. Device deployment and undeployment should be visualized using fluoroscopy. Failure to do so may result in catheter damage and/or patient injury.

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3. Retract the guidewire into the FARADRIVE Sheath.
4. Carefully withdraw the FARAWAVE Catheter, along with the guidewire, from the body through the FARADRIVE Sheath using caution to avoid introducing air into the sheath upon removal.
5. Carefully withdraw the FARADRIVE Sheath from the left atrium in accordance with its IFU.
6. Turn off the PFA Generator.

Disposal

To minimize risk of infection or microbial hazards after use, dispose of device and packaging as follows:

After use, the catheter may contain biohazardous substances. The catheter and packaging should be treated and disposed of as biohazardous waste in accordance with any applicable hospital, administrative, and/or local government regulations. Use of a biohazardous container with biological hazard symbol is recommended. Untreated biohazardous waste should not be disposed of in the municipal waste system.

Post-Procedure

Carefully monitor patient while in recovery to ensure hemostasis is achieved and any complications are immediately treated.

Complaint Reporting

In the event that a serious incident occurred in relation to the device, including all patient deaths for procedures where the FARAPULSE product was used, the event should be reported to Boston Scientific and the appropriate regulatory agency.

Boston Scientific's local contact information may be found at: www.bostonscientific.com

Return any catheter related to a complaint, patient harm, injury, or death to Boston Scientific using a BSC Returned Product Kit.

- Returning products for analysis and providing product performance observations helps drive higher reliability on an ongoing basis.
- Be sure to follow the instructions with regard to packaging and shipping any biohazard devices taking care not to expose the handle or connector to fluid that may compromise the catheter and limit analysis.

PATIENT COUNSELING INFORMATION

The physician should consider the following points while counseling patients on the use of the FARAWAVE Catheter in association with the electrophysiological cardiac interventional procedure:

- Discuss the risks and benefits including review of potential adverse events listed in this document.
- Discuss post procedure instructions, including any lifestyle changes, medications, when to call the Healthcare Provider (HCP) and any post procedure follow-up that might be needed.

WARRANTY

For device warranty information, visit www.bostonscientific.com/warranty.

SYMBOL DEFINITIONS

Commonly used medical device symbols that appear on the labeling are defined at www.bostonscientific.com/SymbolsGlossary.

Additional symbols are defined at the end of this document.

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324H) eIFU, MB, FARAWAVE 2.0 PERSAF, US, en, 51967690-01A

Table 25. Symbol Definitions

	Contents
	Compatible Guidewire OD

Boston Scientific Corporation
300 Boston Scientific Way
Marlborough, MA 01752 USA
USA Customer Service +1-888-272-1001

www.bostonscientific.com

2025-09
< en >

BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324H) eIFU, MB, FARAWAVE 2.0 PERSAF, US, en, 51967690-01A

Black (K) ΔE ≤5.0 / CMYK