SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Pulsed Field Ablation System
Device Trade Name:	FARAPULSE™ Pulsed Field Ablation System (FARAWAVE™ Pulsed Field Ablation Catheter, FARAWAVE™ NAV Pulsed Field Ablation Catheter, FARASTAR™ Catheter Connection Cable, FARASTAR™ Pulsed Field Ablation Generator, FARASTAR™ Recording System Module, FARASTAR™ Mapping System Module, FARASTAR™ Stimulation Module Cable, FARASTAR™ EGM Cable, FARASTAR™ Stimulation Module Male Cable, FARASTAR™ Stimulation Module Female Cable, FARASTAR™ Stimulation Module Y-Cable Long, FARASTAR™ Stimulation Module Y-Cable Short, FARASTAR™ Recording System Module Catheter Pin Cable, FARASTAR™ Recording System Module ECG Trunk Cable, FARASTAR™ Recording System Module ECG Output Module (AAMI/IEC), FARASTAR™ Recording System Module EGM Input Module, FARASTAR™ SNAP CABLE R/L – (AAMI/IEC), FARASTAR™ SNAP CABLE V SET – (AAMI), FARASTAR™ SNAP CABLE C SET – (IEC), FARASTAR™ Recording System Module ECG Output to Rhythmia HDx™ ECG Input Cable, FARASTAR™ Recording System Module EGM Output to Rhythmia HDx™ EGM Input Cable, FARASTAR™ Mapping System Module Back Patch Cable, FARASTAR™ Mapping System Module Back Patch Cable Male, FARASTAR™ Mapping System Module BNC BNC-Phono Cable, FARASTAR™ Mapping System Module Rhythmia™ ABL Cable, FARASTAR™ Mapping System Module Auxiliary Cable)
Device Procode:	QZI
Applicant's Name and Address:	Boston Scientific Corporation 300 Boston Scientific Way Marlborough, MN 01752

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230030/S007

Date of FDA Notice of Approval: July 3, 2025

The original PMA P230030 was approved on January 30, 2024, and is indicated for:

FARAWAVE™ Pulsed Field Ablation Catheter
The FARAWAVE Catheter is indicated for the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

FARASTAR™ Pulsed Field Ablation Generator
The FARASTAR PFA Generator when used in conjunction with the FARAWAVE PFA Catheter, is indicated for the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

FARASTAR™ Recording System Module
The FARASTAR Recording System Module (RSM) is indicated for use in an electrophysiology lab environment, as a filtering/protection unit to be connected between the patient and any attached recording systems and/or ECG systems, and as an interface for cardiac stimulation output.

FARASTAR™ Catheter Connection Cable
The FARASTAR Connection Cable is intended to be used with a FARAPULSE Catheter during an Electrophysiology procedure for cardiac tissue ablation.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the FARAWAVE Pulsed Field Ablation System.

II. INDICATIONS FOR USE

The FARAPULSE Pulsed Field Ablation System is indicated for:

FARAWAVE™ and FARAWAVE™ NAV Pulsed Field Ablation catheters
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).

FARASTAR™ Pulsed Field Ablation Generator
The FARASTAR PFA Generator is intended for use with a compatible Boston Scientific PFA catheter in cardiac ablation procedures.

FARASTAR™ Recording System Module
The FARASTAR Recording System Module (RSM) is indicated for use in an electrophysiology lab environment, as a filtering/protection unit to be connected between the patient and any attached recording systems and/or ECG systems, and as an interface for cardiac stimulation output.

FARASTAR™ Catheter Connection Cable
The FARASTAR Connection Cable is intended to be used with a FARAPULSE Catheter during an Electrophysiology procedure for cardiac tissue ablation.

III. CONTRAINDICATIONS

- 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.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FARAWAVE Pulsed Field Ablation System labeling.

V. DEVICE DESCRIPTION

The FARAPULSE PFA System consists of the FARAWAVE PFA Catheter (NAV and non-NAV), FARASTAR PFA Generator and accessories, FARASTAR RSM and accessories, and FARASTAR MSM and accessories. These components are designed to operate together as a system. The FARASTAR PFA Generator produces PEF energy in the form of discrete high-voltage pulses with a pre-defined waveform and is controlled via a console with an LCD touchscreen display. The FARASTAR PFA Generator is used in conjunction with the FARASTAR RSM, which is used to reduce potential interference to the Electrophysiology Laboratory Recording System during the ablation procedure as well as to provide output connection for synchronous mode operation, and the FARASTAR MSM, which is used to reduce potential interference to the mapping system during ablation. The FARASTAR PFA Generator, FARASTAR RSM, and FARASTAR MSM are non-sterile, reusable, capital equipment whereas the FARAWAVE PFA Catheter is a single use, disposable device.

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.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of drug refractory recurrent symptomatic paroxysmal or persistent atrial fibrillation. These alternatives include:

- Treatment with medicines that help control the rate and/or rhythm of the heart and other medicines that reduce the likelihood of clots forming (known as medical or pharmacologic therapy).
- Cardioversion to restore the heart's normal rhythm (with electrical shock or medicine).
- Ablation of the AV node and insertion of a permanent pacemaker to control the heart rate.
- Implantable devices that reduce the likelihood of clots forming.
- Catheter ablation with other devices approved in the United States.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The FARAPULSE Pulsed Field Ablation System was initially CE Marked on January 26, 2021, and the original PMA (P230030) was approved on January 30, 2024. In addition to being marketed in the European Union, the subject system is marketed in various countries around the world such as Japan, China, South Korea, South Africa, United Arab Emirates (UAE), Andorra, Great Britain, Hong Kong, Israel, Kuwait, Macau, Saudi Arabia, Switzerland, Australia, Singapore, New Zealand, and Malaysia. The products have not been withdrawn from any market for any reason.

The FARAWAVE Catheter (NAV and non-NAV) and FARASTAR MSM components of the FARAPULSE PFA System were approved on October 18, 2024 (P230030/S003).

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- 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 [pulmonary vein] stenosis and its symptoms, for example:
  - Cough
  - Shortness of breath, fatigue
  - Hemoptysis
- Surgical and access site complications, for example:
  - Hematoma/seroma
  - AV [arteriovenous] 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.
- Procedure 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

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

No additional non-clinical studies were conducted to support this PMA supplement. Please refer to the P230030 SSED available on the FDA website for a description of previously conducted non-clinical studies.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study (ADVANTAGE AF Clinical Study Phase 1, ClinicalTrials.gov NCT05443594) to establish a reasonable assurance of safety and effectiveness of catheter ablation with the FARAPULSE Pulsed Field Ablation System for the treatment of drug-refractory, symptomatic, persistent atrial fibrillation (PsAF) in the US, Canada, and Europe under IDE G220079. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between February 28, 2023, and August 30, 2023. The database for this Panel Track Supplement reflected data collected through August 26, 2024, and included 355 patients, 339 of whom were treated with the FARAPULSE Pulsed Field Ablation System. There were 43 investigational sites.

The study was a prospective, single-arm, open-label, multi-center clinical study. All subjects who met the eligibility criteria, signed the informed consent, and underwent the ablation procedure (the "index procedure") were followed for 12 months. Follow-up included twice per month event monitoring plus symptom-driven event monitoring beginning on day 90, a 24-hour Holter monitor (ambulatory electrocardiograph) 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. Arrhythmia recurrence between the index procedure and day 90 were considered within the "blanking period" and did not contribute to the arrhythmia recurrence endpoint. The first subject enrolled by each ablating investigator at each site was considered part of the Roll-In cohort and all other subjects were considered part of the Treatment cohort.

There was no active control group. Results were evaluated against pre-defined performance goals based on the percentage of subjects who experienced arrhythmia recurrence within 12 months and the percentage of subjects who experienced one or more composite serious adverse events.

The study utilized an independent Clinical Events Committee to review and adjudicate adverse events. A core laboratory was used to review the 12-lead ECGs, 24-hour Holter Monitor recordings and transmissions from the study-specific event monitors for adjudication of arrhythmia recurrence.

1. Inclusion and Exclusion Criteria

Enrollment in the ADVANTAGE AF Phase 1 study was limited to patients who met the following inclusion criteria:

1. Age ≥ 18 years of age, or older if specified by local law.
2. Subjects have symptomatic, documented, drug-resistant, Persistent AF, defined as:
    a. **Documented:** at a minimum a physician's note confirming the arrhythmia symptoms and durations AND, within 180 days of Enrollment Date, either:

i. A 24-hour continuous ECG recording confirming continuous AF OR
ii. Two ECGs from any regulatory cleared rhythm monitoring device showing continuous AF taken at least 7 days apart.

b. **Drug-resistant:** effectiveness failure of, intolerance to, or specific contraindication to at least one (1) AAD (Class I or III).

c. **Persistent:** continuous AF for > 7 days and ≤ 365 days.

3. Subjects who are willing and capable of providing informed consent.

4. Subjects who are willing and capable of participating in all testing associated with this clinical investigation at an approved clinical investigational center.

Patients were <u>not</u> permitted to enroll in the ADVANTAGE AF Phase 1 study if they met any of the following exclusion criteria:

1. Any of the following atrial conditions:

   a. Left atrial (LA) anteroposterior diameter ≥ 5.5 cm, or if LA diameter not available, non-indexed volume >100 ml (by MRI [magnetic resonance imaging], CT [computed tomography] or TTE [transthoracic echocardiography] report or physician note).

   b. Any prior atrial endocardial, epicardial or surgical ablation procedure for arrhythmia, other than right sided cavotricuspid isthmus ablation or for right sided SVT [supraventricular tachycardia].

   c. Current atrial myxoma.

   d. Any PV abnormality, stenosis, or stenting (common and middle PVs are admissible).

   e. Current left atrial thrombus

2. Cardiovascular (CV) exclusions – Any of the following CV conditions:

   a. History of sustained ventricular tachycardia or any ventricular fibrillation.

   b. AF that is secondary to electrolyte imbalance, thyroid disease, alcohol, or other reversible / non-cardiac causes.

c. Current or anticipated pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy devices, interatrial baffle, closure device, patch, or patent foramen ovale occluder, LA appendage closure, device or occlusion, active implantable loop recorder or insertable cardiac monitor at the time of ablation.

d. Valvular disease that is any of the following:

   i. Symptomatic.
   ii. Causing or exacerbating congestive heart failure.
   iii. Associated with abnormal LV function or hemodynamic measurements.

e. Hypertrophic cardiomyopathy.

f. Any prosthetic heart valve, ring or repair including balloon aortic valvuloplasty.

g. Any IVC [inferior vena cava] filter, known inability to obtain vascular access or other contraindication to femoral access.

h. Rheumatic heart disease.

i. Congenital heart disease with any clinically significant residual anatomic or conduction abnormality.

j. Awaiting cardiac transplantation or other cardiac surgery within the next 12 months.

3. Any of the following conditions at baseline:

   a. Heart failure associated with NYHA [New York Heart Association] Class III or IV.

   b. LVEF < 40%.

   c. Uncontrolled hypertension (SBP > 160 mmHg or DBP > 95 mmHg on two BP measurements at baseline assessment.

4. Any of the following events within 90 days of the Consent Date:

   a. Myocardial infarction (MI), unstable angina or coronary intervention.

   b. Any cardiac surgery.

c. Heart failure hospitalization.

d. Pericarditis or symptomatic pericardial effusion.

e. Gastrointestinal bleeding.

f. Stroke, TIA [transient ischemic attack], or intracranial bleeding.

g. Any non-neurologic thromboembolic event.

h. Carotid stenting or endarterectomy.

5. Thrombocytosis, thrombocytopenia, disorder of blood clotting or bleeding diathesis.

6. Contraindication to, or unwillingness to use, systemic anticoagulation.

7. Patients who have not been on anticoagulation therapy for at least 4 weeks prior to the ablation procedure.

8. Women of childbearing potential who are pregnant, lactating, not using medical birth control or who are planning to become pregnant during the anticipated study period.

9. Health conditions that in the investigator's medical opinion would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or modify outcome data or its interpretation, including but not limited to:

    a. Body Mass Index (BMI) > 42.0.

    b. Solid organ or hematologic transplant, or currently being evaluated for a transplant.

    c. Any prior history or current evidence of hemi-diaphragmatic paralysis or paresis.

    d. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or requiring supplemental oxygen.

    e. Renal insufficiency if an estimated glomerular filtration rate (eGFR) is < 30 mL / min / 1.73 m^2, or with any history of renal dialysis or renal transplant.

f. Active malignancy or history of treated malignancy within 24 months of enrollment (other than cutaneous basal cell or squamous cell carcinoma).

g. Clinically significant gastrointestinal problems involving the esophagus or stomach including severe or erosive esophagitis, uncontrolled gastric reflux, gastroparesis, esophageal candidiasis or active gastroduodenal ulceration.

h. Active systemic infection.

i. COVID-19 disease.

ii. Current confirmed, active COVID-19 disease.

iii. Current positive test for SARS-CoV-2.

iv. Confirmed COVID-19 disease not clinically resolved at least 3 months prior to the Consent Date.

i. Uncontrolled diabetes mellitus or a recorded HgbA1c > 8.0% in the 90 days prior to the Consent Date

j. Untreated diagnosed obstructive sleep apnea with apnea hypopnea. index classification of severe (>30 pauses per hour).

10. Predicted life expectancy less than 1 year.

11. Subjects who are currently enrolled in another investigational study or registry that would directly interfere with the current study, except when the subject is participating in a mandatory governmental registry, or a purely observational registry with no associated treatments; each instance must be brought to the attention of the Sponsor to determine eligibility

2. Follow-up Schedule

All patients were scheduled for follow-up examinations at pre-discharge, day 7, day 30, day 90, day 180, day 360, and any re-ablation procedure or unscheduled assessments postoperatively. All data collection assessments are depicted in Table 1.

Table 1: Data Collection Assessments

			Blanking Period				Effectiveness Evaluation Period			Other
	Screen/Baseline (In-Person)	Index Procedure (In-Person) Day 0	Pre-Discharge (In-Person)	Day 7 (Remote) Days 7-11	Day 30 (Remote) Days 30-37	Re-Ablation within Blanking	Day 90 (In-Person) Days 90+-14	Day 180 (Remote) Days 180+-30	Day 360 (In-Person Days 360_030	Unscheduled CV (In-Person or Remote)
Informed Consent, Eligibility, Baseline Assessments (including NYHA Class)	X									
Laboratory testing	X		X							
AAD and anticoagulant medications	X		X	X	X	X	X	X	X	X
Recurrent arrhythmia, cardioversions, ablations, hospital admissions			X	X	X	X	X	X	X	X
12-lead ECG	X		X			X	X		X	X
TTE	X									
Cardiac CT/MRI	X					X	X		X	X
Ablation procedure data		X				X				
Event monitors	X						X	X	X	
24-hour continues ECG (Holter)	X							X	X	
TEE/CT/intracardiac echocardiography (ICE) to exclude LA thrombus		X				X				
Radiologic examination of diaphragm		X				X	X		X	
EQ-5D-3L & AFEQT assessments	X							X	X	
Pre-/post-NIHSS	X		X			X				
Neuro assessments			X			X				
Adverse events		X	X	X	X	X	X	X	X	X

3. Clinical Endpoints

The primary safety endpoint 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. The results were evaluated against a performance goal of 12% using the Kaplan-Meier method and a 97.5% one-sided upper confidence limit.

Table 2: Primary Safety Endpoint Assessments

CSAEs	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 was the proportion of Treatment subjects with treatment success through day 360 assessment. The results were evaluated against a performance goal of 40% using the Kaplan-Meier method and a 97.5% one-sided lower confidence limit.

Treatment success was defined as both Persistent AF Acute Procedural Success and Persistent AF Chronic Success.

1. Persistent AF Acute Procedural Success was defined as:

    a. The isolation of all attempted PVs as clinically assess at the end of the procedure by entrance block performed with or without adenosine testing, AND

    b. The isolation of the left atrial posterior wall (PW) as clinically assessed at the end of the procedure, performed with or without adenosine testing, via interrogation by multipolar diagnostic catheter or 3D electroanatomical mapping.

2. Persistent AF Chronic Success was defined as freedom from any of the following through the day 360 assessment after the blanking period, excluding documented cavotricuspid (CTI)-dependent atrial flutter (AFL):

    a. Arrhythmia: Occurrence of any detectable AF, AFL, or atrial tachycardia (AT).

    b. Re-ablation: Any re-ablation for AF, AFL, or AT.

    c. Cardioversion: Any electrical cardioversion for AF, AFL, or AT.

    d. AAD Use: Use of a non-failed Class I / III AAD or amiodarone.

B. Subject Accountability

A total of 355 subjects were enrolled in the study. There were 79 Roll-In subjects, 16 Consent Ineligible or Intent subjects that did not undergo the Index Procedure, and 260 subjects classified as Treatment subjects that underwent an Index Procedure with the FARAPULSE PFA System.

Table 3: Subject Status

Status	Active	Withdrawn	Deceased	Completed Study	Total
Roll-In	**0**	**3**	**0**	**76**	**79**
Treatment	0	3	0	76	79
Non Roll-In	**0**	**27**	**0**	**249**	**276**
Consent Ineligible	0	10	0	0	10
Intent	0	6	0	0	6
Treatment	0	11	0	249	260
Total	**0**	**30**	**0**	**325**	**355**

C. Study Population Demographics and Baseline Parameters

The demographics of the study population were typical for a PsAF catheter ablation study performed in the US. Tables 4 and 5 present the demographics and baseline characteristics for the Treatment subjects.

Table 4: Treatment Subject 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%)
	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 5: Baseline Characteristics

Characteristic	Measurement	Subject Results (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%)
Cerebrovascular Disease History	Cerebral Vascular Accident (CVA)/Stroke	14 (5.4%)
	Transient Ischemic Attack (TIA)	6 (2.3%)

Characteristic	Measurement	Subject Results (N=260)
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	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 Intolerant 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%)
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	

Characteristic	Measurement	Subject Results (N=260)
	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

D. Safety and Effectiveness Results

1. Safety Results

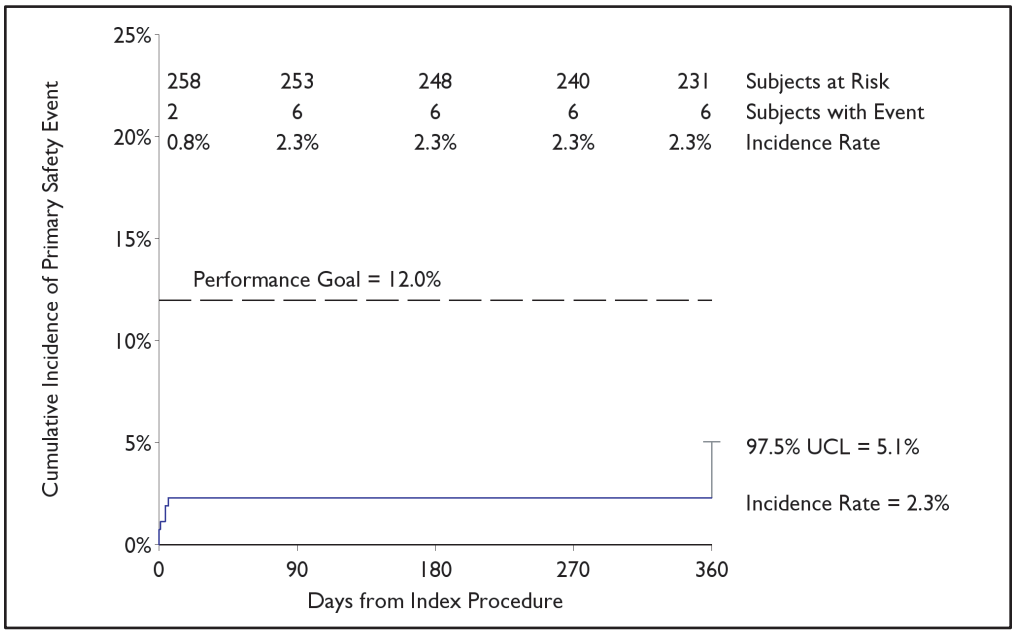
Primary Safety Endpoint

The primary safety endpoint was the proportion of Treatment and Attempt subjects with one or more device- or procedure- related pre-defined Composite Serious Adverse Events (CSAE's) following the Index Procedure/ Rescheduled Index Procedure or the Re-ablation Procedure within Blanking Period.

Per study protocol, the primary safety analysis included Attempt (n = 0) and Treatment subjects (n = 260) in the non-Roll-In population.

Out of 260 Treatment subjects, 6 subjects experienced a device- or procedure-related CSAE through Day 360 for a cumulative primary safety event incidence rate of 2.3% (Figure 1). 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 1. Primary Safety Endpoint Result



The device- or procedure-related CSAEs that occurred following the Index Procedure are summarized in Table 6. Each event was classified by the ADVANTAGE AF Clinical Events Committee (CEC) following pre-defined CSAE definitions.

Table 66: Primary Safety Events

Primary Safety Event Type	Subjects with an Event1 (% of Total Subjects) (N=260) Subjects may experience multiple Primary Safety Endpoint event types
Myocardial Infarction	1 (0.4%)
Pericarditis	1 (0.4%)
Pulmonary edema	4 (1.5%)

Related Serious Adverse Events

There were 22 (8.5%) subjects and 29 total events that were adjudicated as a procedure related serious adverse event by the CEC as shown in Table 7. A subset of these events, shown in Table 8, were also adjudicated as device related. The device related events included 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.

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.

There was one (1) laboratory confirmed hemolysis serious adverse event adjudicated as related to the procedure and another component of the FARAPULSE PFA system but not related to the FARAWAVE catheter or FARADRIVE Steerable Sheath. This subject received 93 total PFA applications and experienced acute kidney injury (with elevation of creatinine from 1.2 to 2.3 mg/dL) secondary to intravascular hemolysis before normalizing with conservative management.

There was one (1) acute coronary syndrome requiring percutaneous coronary intervention and stent placement in the subject with myocardial infarction. It 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.

Table 7: Procedure-related Serious Adverse Events in Treatment Subjects (n = 260)

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%)**	**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	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

Table 8: Device-related Serious Adverse Events in Treatment Subjects (n = 260)

	CEC Adjudication as Serious	
Sponsor AE Classification	**Subjects (%)**	**Events**
Total	**5 (1.9%)**	**5**
Atrial tachycardia/Other SVT	2 (0.8%)	2
Atrial Fibrillation (AF)	1 (0.4%)	1
Hemolysis (Laboratory confirmed)	1 (0.4%)	1
Oozing/Bleeding	1 (0.4%)	1

Death and Unanticipated Adverse Device Effects

There were no deaths or unanticipated adverse effects reported in the ADVANTAGE AF Clinical Study Phase 1.

2. Effectiveness Results

Primary Effectiveness Endpoint

Per study protocol, the primary effectiveness analysis included Treatment subjects (260) in the non-Roll-In population. A subject was classified as primary effectiveness success or treatment success when both acute procedural success and chronic success were achieved.

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.
The second component of the Primary Effectiveness Endpoint was 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 persistent AF Treatment Success rate of 63.5% with a one-sided 97.5% lower confidence limit (LCL) of 57.3%. Since the LCL is greater than the pre-specified performance goal of 40%, the Primary Effectiveness Endpoint was met.

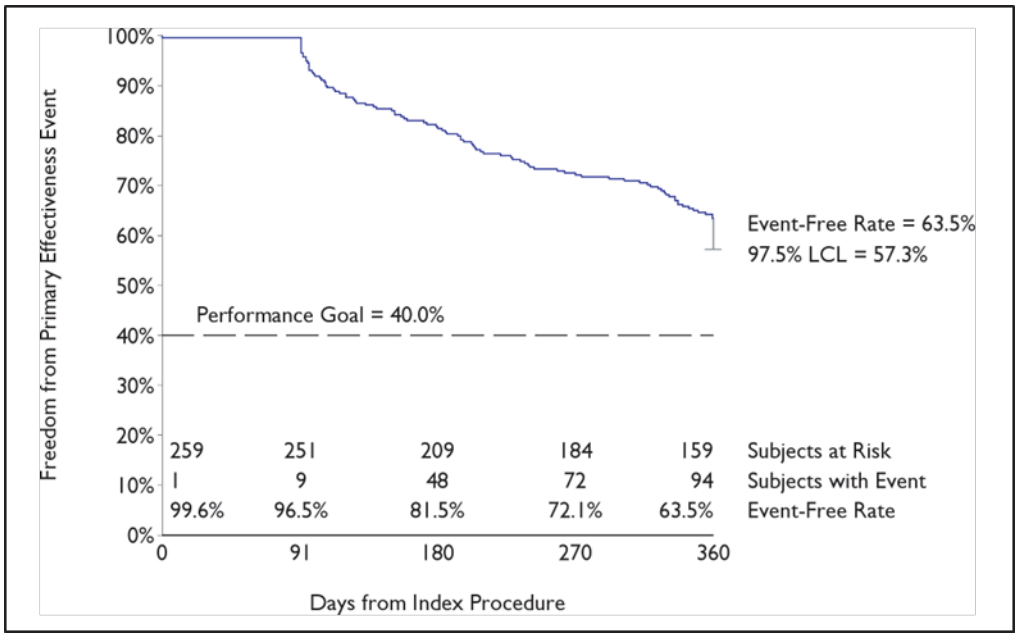


Figure 2. Freedom from Primary Effectiveness Failure at Day 360

The first and subsequent primary effectiveness failure events are summarized in Table 9. 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.

Table 9. 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%)
≥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%)

Additional Effectiveness Analyses

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 Treatment subjects.

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 Treatment subjects.

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 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).

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 recurrences. 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.

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 arrhythmia 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 proportion of subjects free of symptomatic recurrence and intervention to treat arrhythmia recurrence was 85.3%.

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.

3. Subgroup Analyses

   Subgroup analyses were performed for the primary endpoints to determine whether significant differences exist in endpoint results by baseline

demographics, baseline assessments, or procedural characteristics. The following subgroups were pre-specified in the Statistical Analysis Plan: Age (< 65 vs. >= 65), sex, geography (US vs. Outside of the US), BMI (<30 vs. >= 30), baseline LVEF (<60% vs. >= 60%), cardioversion history (<= 1 vs. > 1 prior electrical cardioversion) , LA volume or LA diameter (LV volume <= 70mL vs. >70 mL or LA diameter <= 4.3 cm vs. > 4.3 cm), ablation beyond the PVs, PW, and CTI during the index procedure (Yes vs. No), CTI ablation during the index procedure (Yes vs. No), and event monitor monthly compliance (>= 80% vs. < 80%). Continuous variables were stratified by a pre-specified or clinically meaningful value, when available or otherwise by median value. Additionally, the following subgroup analyses were performed post-hoc: Years since AF diagnosis (<= 1 year vs. > 1 year) and mapping of the PW during the index procedure (Yes vs. No).

Kaplan-Meier estimation was used to calculate the cumulative incidence rate for the Primary Safety Endpoint and the event-free rate for the Primary Effectiveness Endpoint within each subgroup through Day 360, and a log-rank test was used to test for significant difference at a 15% significance level.

There was nominal significant difference in primary effectiveness outcome when assessed by age, sex and cardioversion history with subjects ≥65 years of age, female sex, baseline LVEF < 60% or more than one prior electrical cardioversion being more likely to fail the primary effectiveness endpoint (Table 10). Regarding the primary safety endpoint, a significant difference was found by baseline LVEF, cardioversion history, and additional ablations beyond PVs, PW and CTI during the index procedure (Table 11). The big difference in the primary safety event rate between subjects with additional ablations and those without was likely caused by chance because only a very small number of subjects received additional ablations beyond PVs, PW and CTI in the study.

Table 10: Subgroup Analyses for Primary Effectiveness Endpoint

Covariate	Subgroup	N	Event-Free Rate (95% CI)	p-Value[2]
Age	<65 years	103	73.5% (63.7%, 81.0%)	0.008
	>= 65 years	157	56.9% (48.8%, 64.3%)	
Sex	Female	80	51.9% (40.4%, 62.2%)	0.016
	Male	180	68.6% (61.2%, 74.9%)	

Geography	United States	228	64.5% (57.9%, 70.4%)	0.32
	Outside of the U.S.	32	56.3% (37.6%, 71.3%)	
BMI	<30 kg/m2	132	67.1% (58.4%, 74.5%)	0.32
	>=30 kg/m2	128	59.7% (50.5%, 67.6%)	
LVEF	<60%	138	58.2% (49.5%, 66.0%)	0.061
	>=60%	121	69.1% (60.0%, 76.6%)	
Cardioversion history	<=1 prior cardioversion	169	68.7% (61.1%, 75.2%)	0.010
	>1 prior cardioversion	91	53.8% (43.0%, 63.4%)	
LA volume or LA diameter	At or below the median[1]	134	63.0% (54.2%, 70.6%)	0.81
	Above the median[1]	126	64.0% (54.9%, 71.7%)	
Ablation beyond PVs, PW, and CTI during Index Procedure	No additional ablations	251	64.1% (57.8%, 69.8%)	0.086
	Additional ablations	9	44.4% (13.6%, 71.9%)	
CTI Ablation during Index Procedure	No CTI ablation	210	64.4% (57.4%, 70.5%)	0.58
	CTI ablation	50	59.6% (44.6%, 71.8%)	
Event monitor monthly compliance	<80%	131	65.9% (57.1%, 73.4%)	0.43
	>=80%	129	61.0% (52.0%, 68.8%)	
Years since AF diagnosis	<=1 year	156	65.7% (57.6%, 72.6%)	0.22
	>1 year	104	60.1% (49.9%, 68.8%)	
Mapping of PW during Index Procedure	No PW mapping	65	65.8% (52.8%, 76.0%)	0.60
	PW mapping	195	62.7% (55.5%, 69.1%)	

N = Treatment subjects in subgroup; CI = confidence interval
[1]Median LA volume = 70mL; Median LA diameter = 4.3cm
[2]P-values are not adjusted for multiple comparisons and should be interpreted with caution

Table 11: Subgroup Analyses for Primary Safety Endpoint

Covariate	Subgroup	N	Cumulative Incidence Rate (95% CI)	p-Value[2]
Age	<65 years	103	1.0% (0.1%, 6.7%)	0.25
	>= 65 years	157	3.2% (1.3%, 7.5%)	
Sex	Female	80	1.2% (0.2%, 8.5%)	0.45
	Male	180	2.8% (1.2%, 6.5%)	
Geography	United States	228	2.2% (0.9%, 5.2%)	0.73
	Outside of the US	32	3.1% (0.4%, 20.2%)	
BMI	<30 kg/m2	132	2.3% (0.7%, 6.9%)	0.96
	>= 30 kg/m2	128	2.3% (0.8%, 7.1%)	
LVEF	<60%	138	3.6% (1.5%, 8.5%)	0.14
	>= 60%	121	0.8% (0.1%, 5.7%)	
Cardioversion history	<=1 prior cardioversion	169	1.2% (0.3%, 4.6%)	0.097
	>1 prior cardioversion	91	4.4% (1.7%, 11.3%)	
LA volume or LA diameter	At or below the median[1]	134	2.2% (0.7%, 6.8%)	0.95
	Above the median[1]	126	2.4% (0.8%, 7.2%)	
Ablations beyond PVs, PW, and CTI during Index Procedure	No additional ablations	251	2.0% (0.8%, 4.7%)	0.074
	Additional ablations	9	11.1% (1.6%, 56.7%)	
CTI Ablation during Index Procedure	No CTI ablation	210	2.4% (1.0%, 5.6%)	0.87
	CTI ablation	50	2.0% (0.3%, 13.4%)	
Years since AF diagnosis	<=1 year	156	2.6% (1.0%, 6.7%)	0.74
	>1 year	104	1.9% (0.5%, 7.5%)	
Mapping of PW during Index Procedure	No PW mapping	65	0.0% (0.0%, 0.0%)	0.15
	PW mapping	195	3.1% (1.4%, 6.7%)	

N = Treatment subjects in subgroup; CI = confidence interval
[1]Median LA volume = 70mL; Median LA diameter = 4.3cm
[2]P-values are not adjusted for multiple comparisons and should be interpreted with caution

Multivariable analysis was performed to assess the impact of multiple covariates on the Primary Effectiveness Endpoint. Multivariable analysis was not performed for the Primary Safety Endpoint due to the number of events being

too small to detect meaningful differences between subgroups, particularly when assessing multiple subgroups in a single model.

The covariates under consideration for the multivariable analysis of the Primary Effectiveness Endpoint were described above. Variables found to be significantly associated with the outcome in a univariable Cox proportional hazards model at the 0.15 significance level were included in a multivariable Cox proportional hazards model. Backwards selection with a 0.15 alpha exit criterion was used to determine the final multivariable model for the Primary Effectiveness Endpoint through Day 360.

Age >= 65 years, female sex, baseline LVEF <60%, more than one (1) prior cardioversion, and additional ablations (beyond PVs, PW, and CTI) were significant predictors of Treatment Failure in the univariable analysis, and all but additional ablations remained significant in the multivariable model.

4. Pediatric Extrapolation

   In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 87 investigators of which 0 were full-time or part-time employees of the sponsor and 13 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 13
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness outcomes of the ADVANTAGE AF Phase 1 study demonstrated a reasonable assurance that the FARAPULSE Pulsed Field Ablation System is effective for the treatment of symptomatic drug refractory persistent AF.

The clinical study met its primary effectiveness objective. The observed primary effectiveness success rate was 63.5%. The lower one-sided 97.5% confidence limit of 57.3% exceeded the predefined performance goal of 40% derived from the minimum chronic acceptable success rate recommended in the Heart Rhythm Society Expert Consensus Statement on Catheter and Surgical Ablation of AF. The primary effectiveness success rate reported in the study is in line with that reported in recent IDE studies that supported the approval of several ablation catheters for the treatment of symptomatic drug refractory persistent AF.

The clinical study also showed that ablation was associated with an improvement in the quality-of-life (QoL) scores. Although a placebo effect cannot be excluded without a sham control arm, the finding of sustained and clinically significant improvements in QoL scores over one year post procedure was supportive of a QoL treatment benefit in this group of symptomatic patients whose quality of life was impaired by AF. The favorable QoL results were further corroborated by a high rate (85.3%) of freedom from symptomatic arrhythmia recurrence reported in the study. Subgroup analyses suggested that older patients, women and those with a lower baseline LVEF or multiple prior electrical cardioversions might derive less benefit from catheter ablation. Advanced age, female sex and lower baseline LVEF are known risk factors for arrhythmia recurrence after AF ablation. It has also been reported in the literature that patients who have undergone repeat electrical cardioversions are less likely to maintain normal sinus rhythm despite escalating use of ablation and antiarrhythmic drug therapies. It is reassuring that the treatment success in the subgroups of older subjects, female subjects, subjects with a lower baseline LVEF and those with multiple prior electrical cardioversions still exceeded the minimum chronic acceptable success rate recommended in the consensus statement.

B. Safety Conclusions

The risks of the device are based on data collected in the clinical study conducted to support PMA approval as described above. The ADVANTAGE AF Phase 1 study met its pre-defined safety performance goal. The observed primary safety event rate of was 2.3% with an upper one-sided 97.5% confidence limit of 5.1%.

The reported primary safety events included one myocardial infarction, one pericarditis, and four pulmonary edema events. There were no unanticipated adverse device effects or device or procedure-related death, stroke, severe PV stenosis, or esophageal perforating complications. Of note, there was no coronary spasm (a PFA-specific complication) reported in the study. And only 0.4% of the Treatment subjects (1/260) had hemolysis-related acute kidney injury, another PFA-specific complication confirmed by hemolysis biomarkers. The rate of procedure-related acute kidney injury was estimated to be 0.8% (2/260 Treatment subjects).

Taken together, the safety results of the clinical study demonstrated that the risk of major complications associated with the use of the study device for PV isolation and left atrial PW isolation was low. The frequency, severity and type of procedural complications reported in the study were in line with the published literature of catheter ablation of persistent AF. Moreover, the risks of coronary spasm and hemolysis-related acute kidney injury, two PFA-specific complications appeared to be low, acknowledging that hemolysis biomarkers were not systemically tested in the clincal study.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the ADVANTAGE AF Phase 1 study conducted to support PMA approval as described above. The primary effectiveness endpoint results supported the treatment benefit of reducing atrial tachyarrhythmia recurrence in patients with symptomatic drug refractory persistent AF. Freedom from atrial tachyarrhythmia recurrence, an accepted surrogate for improvement in patient's quality of life and AF-related symptoms in the study population was achieved in the majority of study participants during the 9-month effectiveness evaluation period. This was accompanied by sustained and clinically meaningful improvement in patient's quality-of-life measures.

The probable risks of the device are also based on data collected in the ADVANTAGE AF Phase 1 study conducted to support PMA approval as described above. The safety data from the clinical study supports the notion that the subject device's safety profile when used for PV isolation and left atrial PW isolation is clinically acceptable. The primary safety event rate reported in the study was within the range of the major complication rates reported in the contemporary AF ablation studies. The risks of coronary spasm and hemolysis-related acute kidney injury, two PFA-specific complications appeared to be low based on the clinical study results.

None of the subjects with laboratory-confirmed hemolysis or suspected hemolysis required dialysis or blood transfusion.

No new or unanticipated adverse device effects or patient risks were identified in the ADVANTAGE AF Phase 1 study.

Patient Perspective

The submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for the treatment of drug-refractory symptomatic persistent AF (episode duration less than one year), the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIV. CDRH DECISION

CDRH issued an approval order on July 3, 2025. The final clinical conditions of approval cited in the approval order are described below.

The ADVANTAGE Post-Approval Study (PAS) is a prospective, multi-center, non-randomized, observational study to evaluate the long-term effectiveness and safety of the FARAPULSE Pulsed Field Ablation System and the FARAWAVE Catheter for the treatment of drug-refractory, symptomatic, persistent atrial fibrillation (PsAF). Adult patients who intend to undergo their de novo catheter ablation procedure using the FARAPULSE Pulsed Field Ablation System to treat symptomatic persistent atrial fibrillation (episode duration less than one year) refractory or intolerant to at least one Class I or III antiarrhythmic medication will be enrolled and ablated using the FARAPULSE Pulsed Field Ablation System and the FARAWAVE Catheter. The study will enroll at least 350 study subjects with all patients treated in the United States. The study will aim to include a diverse (i.e., race, ethnicity, gender) patient population. Following consent, all study subjects will complete an enrollment/baseline visit, ablation procedure, and be followed through at least 1 year post-ablation. At least 100 study subjects will be followed through 3 years post-ablation. A 24-hour Holter or equivalent rhythm monitoring will be performed at 6- and 12-months post ablation for asymptomatic recurrence and at times needed for symptomatic recurrences, and for the extended follow-up, annually at 24- and 36-months post-ablation.

The primary objectives of the PAS will be the following:

1. Estimating the primary safety adverse event rate at 3 months following ablation procedure using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

2. Estimating the 12-month freedom from atrial fibrillation (AF)/atrial flutter (AFL)/atrial tachycardia (AT) recurrence following ablation procedure using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

Secondary/Additional objectives will include but are not limited to:

a. Estimating 36-months freedom from AF/AFL/AT recurrence following ablation procedure using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

b. Estimating the rate of procedure-related acute kidney injury through 3 months post-procedure.

c. Estimating the rate of hemolysis-related acute kidney injury requiring intervention through 3 months post-procedure.

d. Estimating the rate of procedure-related pulmonary edema or heart failure events through 3 months post-procedure.

e. Estimating the rate of serious device or serious procedure related adverse events through 12 months post-ablation using the using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

f. Estimating the rate of major procedural complications in patients of 65 years of age or older.

g. Estimating 24-months and 36-months freedom from AF/AFL/AT recurrence following ablation procedure using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

h. Estimating freedom from AF/AFL/AT recurrence and off Class I and III antiarrhythmic medications at 12-, 24-, and 36-months following ablation procedure using the FARAWAVE Catheter and FARAPULSE Pulsed Field Ablation System.

i. Characterizing procedural data that may include but are not limited to procedure time, fluoroscopy time, total number of PF applications, fluid administered intraprocedural, ablation strategy and anesthesia technique.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.