Statistical Analysis Plan (SAP)

The AdmIRE Study
Assessment of Safety and Effectiveness in Treatment Management of Atrial Fibrillation with the BWI IRE Ablation System (BWI201910)

Protocol Version: 4.0

SAP Revision: 1
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Sponsor: BIOSENSE WEBSTER, INC.
31 Technology Dr.
Suite 200
Irvine, CA 92618
USA

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The following individuals have reviewed this version of the Statistical Analysis Plan and are in agreement with the content:

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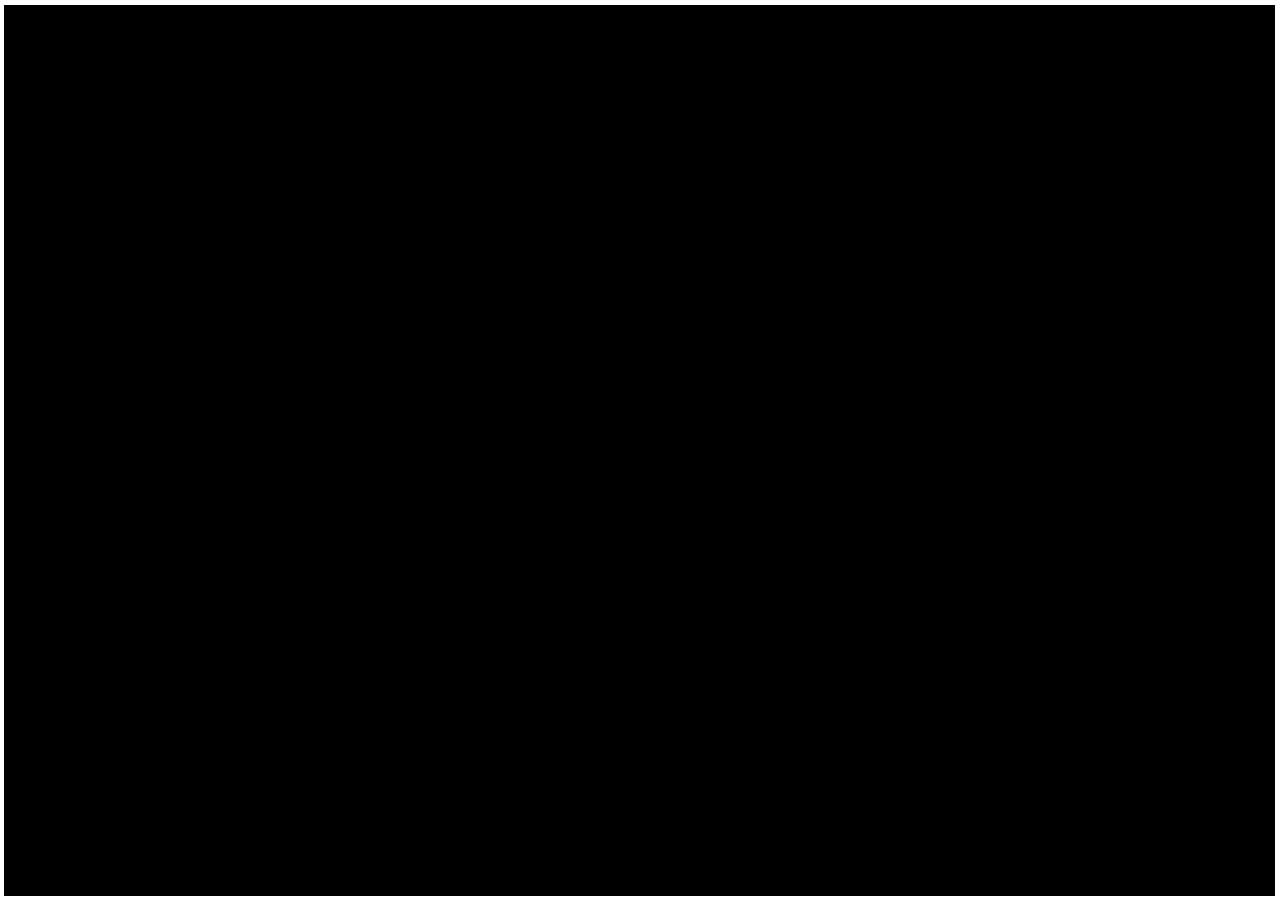

Revision History

Revision Number	Revision Date (DD/MM/YYYY)	Reasons for Revision
1	09/13/2023	Original document using SAP template version 5.0

List of Acronyms and Abbreviations

AAD	Anti-Arrhythmic Drugs
AF	Atrial Fibrillation
AFEQT	Atrial Fibrillation Effect on Quality-of-Life Questionnaire
AFL	Atrial Flutter
AT	Atrial Tachycardia
BWI	Biosense Webster
CCS-SAF	Canadian Cardiovascular Society – Severity of Atrial Fibrillation
CEM	Cardiac Event Monitor
CTI	Cavotricuspid isthmus
CV	Cardiovascular
CVA	Cerebrovascular Accident
DCCV	Direct Current Cardioversion
DMC	Data Monitoring Committee
ECG	Electrocardiogram
FPI	First Pass Isolation
HRQoL	Health Related Quality of Life
IRE	Irreversible Electroporation
mITT	Modified Intent-to-Treat
NSC	Non-Study Catheter
PAF	Paroxysmal Atrial Fibrillation
PEE	Primary Effectiveness Endpoint
PFA	Pulse Field Ablation
PP	Per Protocol
PV	Pulmonary Vein
PVI	Pulmonary Vein Isolation
QOL	Quality of Life
RF	Radiofrequency
SA	Safety Analysis Set
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
TIA	Transient Ischemic Attach
UADE	Unanticipated Adverse Device Effect

Contents

1 Study Design

This clinical investigation is an interventional, prospective, multicenter, non-randomized, single arm, premarket clinical evaluation of the Biosense Webster (BWI) Irreversible Electroporation (IRE) Ablation System (VARIPULSE™ Catheter and TRUPULSE™ Generator) to demonstrate safety and long-term effectiveness when compared to predetermined performance goals. The study will enroll subjects with drug refractory, symptomatic paroxysmal atrial fibrillation (PAF) who are candidates for catheter ablation in two sequential phases, including 1) a Pilot phase which will be used to characterize the safety profile of the BWI IRE system, and 2) a Pivotal phase which will consist of roll-in subjects to verify consistent workflow for use of the IRE system and to minimize the learning curve effect on the evaluation of safety and effectiveness of the system. The main phase subjects will be used for hypothesis testing.

For the purpose of characterization of acute safety, the Pilot phase will enroll 20 evaluable subjects from a protocol-specified maximum of 40 sites in the United States. Enrollment for the Pivotal phase will be initiated when all Pilot phase subjects have at least 30 days of follow-up, unless the Sponsor deems otherwise per section 22 (Study Suspension or Termination) of the study protocol.

The Pivotal phase of this study, roll-in and main phases combined, will enroll a maximum of 408 subjects from up to 40 sites in the United States. The Pivotal roll-in phase will enroll a maximum of 160 subjects. [redacted] The Pivotal main phase will enroll 248 subjects (225 evaluable subjects plus 10% attrition). Data for roll-in subjects will be analyzed separately from the main phase and will not be counted towards the enrollment cap of 225 evaluable subjects of the Pivotal main phase.

After the study ablation procedure, subjects will be followed up for 12 months, including a 3-month blanking period (Day 0-90) and followed by a 9-month evaluation period (Day 91-365). All subjects will be evaluated at 7 days, 1, 3, 6, and 12 months following the index procedure. There will be no formal interim analysis (sample size analysis or early success analysis) in this study.

2 Treatment Assignment

All subjects will be treated with the IRE Ablation System, which includes the multichannel generator (TRUPULSE™) and circular multielectrode catheter (VARIPULSE™).

3 Randomization and Blinding Procedures

This is a single-arm non-randomized trial with all subjects undergoing ablation procedure with the IRE ablation system. Therefore, masking of treatment assignment for operators and subjects is not applicable.

This study will employ several measures to minimize operational bias:

- Screening logs will be maintained at sites to confirm eligible subjects are considered for participation in the study.
- Sponsor personnel directly involved in the conduct of the study will not have access to intermediate aggregated summaries of primary safety and effectiveness endpoint data (from the Pivotal main phase) until preparation for filing for approval.

4 Interval Windows

Subjects will undergo a 3-month blanking period (Day 0-90) followed by a 9-month evaluation period (Day 91-365) and will be scheduled for evaluation at 7 days, 1, 3, 6, and 12 months following the index procedure per the table below. Discontinued subjects who had the study catheter inserted but do not undergo PFA delivery will remain in follow-up for safety for 3 months post catheter insertion and then will be discontinued from the study. All study intervals are calculated from the date of the index procedure (Day 0). Details of the pre- and post-procedure scheduled assessment are provided in the protocol.

	Pre-Procedure	Ablation/Discharge		Phone/Virtual	Follow-Up Visits			
Visit	Screening/Baseline	Study Index Procedure Day 0	Discharge	7D (D7-10)	1M (D23-37)	3M (D76-104)	6M (D150-210)	12M (D335-395)
Visit no.	1	2	3	4	5	6	7	8

5 Levels of Significance

For the Pilot phase and the Pivotal roll-in phase, no formal statistical hypothesis will be formulated or performed.

For the Pivotal main phase, the Type I error for each of the primary endpoints is controlled at a one-sided 2.5% level. The secondary endpoint will only be tested if the primary endpoints are met. The Family-wise error rate for the primary and secondary hypothesis tests will be

controlled at a level of 2.5% by using this gatekeeping strategy. All confidence intervals will utilize a two-sided 95% confidence level unless otherwise specified.

6 Analysis Sets

The analysis sets in this study are defined as the following:

6.1 Pilot Phase

- **Safety Analysis Set (SA):** [redacted]

6.2 Pivotal Phase

6.2.1 Pivotal Main Phase

- **Safety Analysis Set (SA):** [redacted]
- **Modified Intent-To-Treat (mITT) Analysis Set**: [redacted]
- **All Treated Analysis Set**: [redacted]
- **Per Protocol (PP) Analysis Set**: [redacted]
  - [redacted]
    - [redacted]
    - [redacted]

[redacted]

6.2.2 Pivotal Roll-In Phase

- **Roll-In Analysis Set:** [redacted]

7 Sample Size Justification

- **Pilot Phase:**
  As the Pilot phase of the study is a safety characterization phase, a sample size of **20 evaluable subjects** is intended to provide preliminary estimates for safety and acute effectiveness of the IRE Ablation System.

- **Pivotal Main Phase:**
  [redacted]

- [redacted]

- [redacted]

- **Total Sample Size:**
  The sample size is mainly driven by the hypothesis test for the primary effectiveness endpoint. The sample size of **225 evaluable subjects** will provide above 80% power to declare success for each endpoint using an exact binomial test at a one-sided target alpha of 0.025.

8 Statistical Analysis Methods

For the Pilot phase and the Pivotal roll-in phase, data will be analyzed separately (not part of the primary hypothesis testing). No formal statistical hypothesis testing will be conducted, and all analyses will be descriptive. The following confidence intervals will be presented:

- Exact two-sided 95% confidence intervals for primary safety and primary and secondary effectiveness endpoints.
- Two-sided 95% confidence intervals using Greenwood's variance for Kaplan-Meier estimates for long-term effectiveness endpoints.

8.1 General Conventions

Standard descriptive summaries for continuous data include the number of observations with data, mean, standard deviation, median, 25th percentile, 75th percentile, minimum, and maximum values. For categorical data, the count and percent will be presented. Percentages will be based on the number of subjects without missing data.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

8.2 Disposition of Study Subjects

Disposition and accountability of the study subjects will be summarized descriptively for the subject categories defined in section 10.6 of the study protocol.

8.3 Demographic and Baseline Characteristics

Subject demographics, medical history, previously failed AADs, active AAD use at baseline, and other baseline data will be summarized descriptively for subjects in the Pilot SA, Pivotal main study SA, mITT, and PP, and Pivotal Roll-In analysis sets.

8.4 Endpoint(s) and Associated Hypotheses

8.4.1 Primary Endpoint(s)

8.4.1.1. Primary Safety Endpoint

The primary safety endpoint is the occurrence of early onset PAEs (within 7 days of an ablation procedure which uses the VARIPULSE™ Catheter and TRUPULSE™ Generator per protocol, including initial and repeat procedures).

PAEs include the following adverse events (AEs):

Atrio-Esophageal Fistula*	Phrenic Nerve Paralysis (permanent)[+]
Cardiac Tamponade**,***/perforation**	Pulmonary Vein Stenosis[++]
Device or procedure related death[†††]	Stroke/Cerebrovascular Accident (CVA)[†,††]
Major Vascular Access Complication/Bleeding	Thromboembolism
Myocardial Infarction	Transient Ischemic Attack (TIA)
Pericarditis	Pulmonary Edema (Respiratory Insufficiency)
Heart Block	Vagal Nerve Injury/ Gastroparesis

*Atrio-esophageal fistula occurring up to 90 days post atrial fibrillation (AF) ablation procedure will be considered a PAE.

**Cardiac Tamponade/Perforation occurring up to 30 days post AF ablation procedure will be considered a PAE.

*** Hemodynamic compromise or instability is defined as systolic blood pressure < 80 mm Hg.

[+] Absent phrenic nerve function as assessed by a sniff test. Refer to Table 14.2.1.1 in the protocol for permanent phrenic nerve paralysis definition.

[++] Pulmonary vein stenosis occurring anytime during the 12-month follow up period will be considered a PAE.

[†] Non-focal global encephalopathy requires unequivocal evidence based upon neuroimaging studies to be reported as a stroke.

[††] Modified Rankin score assessments should be made by certified individuals.

[†††]Device or procedure-related death anytime during or after the ablation procedure.

The PAE rate will be compared against a performance goal of 12% by testing the following hypothesis:

$$H_0: p_s \geq 0.12 \qquad vs \qquad H_A: p_s < 0.12\,,$$

Where p_s is the proportion of subjects with PAE.

8.4.1.2. **Primary Effectiveness Endpoint**

The primary effectiveness endpoint is freedom from documented (symptomatic and asymptomatic) atrial tachyarrhythmia (atrial fibrillation [AF], atrial tachycardia [AT], or atrial flutter [AFL] of unknown origin^{+}) episodes based on electrocardiographic data (≥30 seconds on an electrocardiogram [ECG], sponsor-provided cardiac event monitor [CEM], or Holter device) during the effectiveness evaluation period (Day 91-365 post index procedure) and freedom from the following failure modes:

- **Acute procedural failure**, defined as failure to confirm entrance block in all pulmonary veins (except those that are silent and/or cannot be cannulated post-procedure) at the end of the procedure.

- **Repeat ablation failure**, including:
  - More than 1 repeat ablation procedures for AF/AT/AFL of unknown origin^{+} during the 3-Month Blanking Period (Day 0-90 post index procedure).
  - Any repeat ablation procedure for AF/AT/AFL of unknown origin^{+} during the evaluation period.

- **Non-study catheter failure**, including:
  - Use of a NSC to treat pulmonary vein targets to achieve isolation of clinically relevant PVs (all PVs except those that are silent and/or cannot be cannulated) and/or to ablate left atrial non-PV AF targets during the index procedure.
  - Use of a NSC to treat pulmonary vein targets to achieve isolation of clinically relevant PVs (all PVs except those that are silent and/or cannot be cannulated) during repeat procedure in the blanking period.

- **AAD failure**, defined as taking a new Class I/III AAD for atrial tachyarrhythmia (AF, AT or AFL of unknown origin^{+}) or taking a previously failed Class I/III AAD at a greater than the highest ineffective historical dose for AF/AT/AFL beyond the 3-month follow-up visit window (i.e., at any time from day 105-365 post index procedure).

- **Continuous AF/AT/AFL of unknown origin^{+}** on a standard 12-lead ECG during the effectiveness evaluation period.

- **Any Direct Current Cardioversion (DCCV) procedure** during the evaluation period for documented atrial tachyarrhythmia (AF, AT or AFL of unknown origin^{+}) recurrences ascertained through protocol specified arrhythmia monitoring methods (12-lead ECG, CEM and Holter monitor).

[+]AFL of unknown origin is defined as all AFL except those cavotricuspid isthmus (CTI) dependent AFL as confirmed by 12-Lead ECG and entrainment maneuvers in an EP study.

The primary effectiveness endpoint will be assessed by testing the following hypothesis:

$$H_0: p_E \leq 0.50 \qquad vs \qquad H_A: p_E > 0.50\,,$$

Where p_E is the proportion of subjects that are free from primary effectiveness failures at 12-month follow-up.

8.4.2 **Secondary Endpoint**

The secondary endpoint is the improvement in quality of life (QOL) of subjects after the ablation procedure. This endpoint will be measured by comparing the Atrial Fibrillation Effect on Quality-of-Life (AFEQT™) scores of subjects before and 12 months after the procedure.

The AFEQT™ includes 20 questions on a 7-point Likert scale. Questions 1-18 evaluate Health Related Quality of Life (HRQoL) and questions 19-20 relate to patients' satisfaction with treatment. The first 18 questions are used to calculate the overall AFEQT score and the subscale scores across three domains as follows:

- AF related Symptoms: Four questions (1 – 4)
- Daily Activities: Eight questions (5 – 12)
- Treatment Concerns: Six questions (13 – 18)

[redacted]

Overall and subscale scores range from 0 to 100. A score of 0 corresponds to complete disability, while a score of 100 corresponds to no disability.

Overall AFEQT scores assessed at baseline and at 12 months post procedure will be compared to see if QOL improved after treatment by testing the following hypothesis:

$$H_0: \mu_d \leq 0 \qquad vs \qquad H_A: \mu_d > 0\,,$$

where μ_d is the average change of the overall AFEQT scores between baseline and 12-month follow-up ($AFEQT_{12M} - AFEQT_{Baseline}$).

8.4.3 Additional Endpoints

No formal hypothesis testing will be performed for additional endpoints.

8.4.3.1. Additional Safety Endpoints

- Incidence of Unanticipated Adverse Device Effects (UADEs).
- Incidence of Serious Adverse Events (SAEs) within 7 days (early-onset), >7 to 30 days (peri-procedural), and >30 days (late onset) of initial ablation/repeat procedure, separately for each timeframe. SAEs that are deemed PAEs will be reported separately and will not be reported as part of the SAE estimates.
- Incidence of bleeding complication (ISTH definitions): a) major bleeding, b) clinically relevant non-major bleeding and c) minor bleeding.

The definition of SAEs can be found in section 14.2.2 of the study protocol. The ISTH bleeding complications definitions can be found in Appendix III (Study Definitions) of the study protocol.

8.4.3.2. Additional Effectiveness Endpoints

- **Acute procedural success**: Defined as the achievement of electrical isolation in all clinically relevant targeted PVs as evidenced by the confirmation of entrance block at the end of the index procedure. Use of a non-study catheter to achieve pulmonary vein isolation (PVI) due to an IRE-system malfunction is considered an acute procedural failure.

- **Acute reconnection:** Defined as the restoration of electrical conduction in any clinically relevant targeted PV as identified by adenosine/isoproterenol challenge during the index procedure.

- **First pass isolation (FPI):** Defined as the achievement of entrance block in all clinically relevant targeted PVs after first encirclement, evaluated prior to the adenosine challenge during the index procure.

- **Touch-up by NSC:** Defined as the use of a NSC to achieve PVI in any clinically relevant targeted PV during the index procedure.

- **Repeat ablation procedures** for AF/AT/AFL of unknown origin during the 12-month follow-up period will be assessed. The evaluation will include the timing of repeat ablation (blanking period or evaluation period), any reconnections of PVs previously isolated during the index procedure, and the type of arrhythmia(s) treated during the repeat ablation, along with their corresponding targets.

- **Freedom from documented (symptomatic and asymptomatic) atrial tachyarrhythmia off Class I/III AAD:** Defined as freedom from documented (symptomatic and asymptomatic) atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365). Taking any Class I/III AAD for AF/AT/AFL of unknown origin beyond the 3-month visit window (i.e., any time from Day 105-365 post index procedure) will also be deemed a failure.

- **12 Month Single Procedure Treatment Success:** Defined as freedom from documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365) following a single index ablation procedure with all other failure modes included.

- **Clinical Success:** Defined as freedom from documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365).

- **Canadian Cardiovascular Society – Severity of Atrial Fibrillation (CCS-SAF):** Defined as improvement in scores of Class 0 to Class 4 at 12 months post procedure compared to baseline.

- **Reduction in Cardiovascular (CV) Hospitalization:** Defined as reduction in CV hospitalization 12 months post procedure (not including repeat procedures) compared to 6 months prior to enrollment.

- **Reduction in DCCV:** Defined as reduction in DCCVs 12 months post procedure compared to 6 months prior to enrollment.

- **AAD Utilization by Timing:** Defined the proportion of subjects on AADs by timing compared to baseline.

8.4.3.3. **Additional Procedural Data**

- Total procedure time, PVI time, PFA application time, mapping time, and PFA application time per lesion
- Total Fluoroscopy Time
- Ablation parameters per application
- Device(s) utilized (per ablation)

8.5 **Analysis of Primary Endpoint(s)**

8.5.1 **Analysis of Primary Safety Endpoint**

In the Pilot phase and the Pivotal roll-in phase, the primary safety endpoint will be summarized descriptively using the total number of PAEs, the number of subjects who experience PAEs, and the percentage of subjects who experience PAEs. The SA will be used to analyze the PAE data from the Pilot phase, while the Roll-In analysis set will be used to analyze the safety data from the Pivotal roll-in phase.

In the Pivotal main phase, hypothesis testing will be performed in the mITT analysis set. Subjects with non-missing PAE outcome data will be included in the primary analysis. The primary safety endpoint will be evaluated using the exact test for a binomial proportion at a one-sided significance level of 2.5%. If the upper bound of the exact two-sided 95% confidence interval of the primary safety endpoint rate is less than the performance goal of 12%, the study will be considered to have demonstrated safety.

To investigate the robustness of the analysis result, sensitivity analyses including estimation of the PAE rate in the SA, worst-case and best-case scenario analyses, and tipping point analysis will be performed in the SA and mITT analysis sets. Details are provided in Section 8.6.

8.5.2 **Analysis of Primary Effectiveness Endpoint**

In the Pilot phase and the Pivotal roll-in phase, the primary effectiveness endpoint will be summarized descriptively as the number and percentage of subjects free from primary effectiveness failure. The SA will be used to analyze the primary effectiveness endpoint data from the Pilot phase and the Roll-In analysis set will be used to analyze the data from the Pivotal roll-in phase.

In the Pivotal main phase, hypothesis testing will be performed in the PP analysis set. Subjects with non-missing primary effectiveness endpoint (PEE) outcome data will be included in the primary

analysis. The primary effectiveness endpoint will be evaluated using the exact test for a binomial proportion at one-sided significance level of 2.5%. If the lower bound of the exact two-sided 95% confidence interval of the primary effectiveness success rate is greater than the performance goal of 50%, the study will be considered to have demonstrated effectiveness.

[redacted]

To investigate the robustness of the analysis result, sensitivity analyses including estimation of the primary effectiveness success rate in the mITT and All Treated analysis sets, worst-case and best-case scenario analyses, tipping point analysis, and Kaplan-Meier estimation will be performed in the PP, All Treated, and mITT analysis sets. Details are provided in Section 8.6.

8.5.3 **Criteria for Study Success**

The study will be considered a success if both primary safety and effectiveness endpoints are met.

8.6 **Sensitivity Analyses**

8.6.1 **Primary Safety Endpoint**

The following sensitivity analyses will be performed in the Pivotal main study SA and mITT analysis sets unless otherwise specified:

- **Sensitivity to Analysis Set**
  [redacted]

- **Best-case Scenario**
  [redacted]

- **Worst-case Scenario**

[redacted]

- **Tipping Point Analysis**

[redacted]

8.6.2 Primary Effectiveness Endpoint

The following sensitivity analyses will be performed in the Pivotal main study mITT, All Treated, and PP analysis sets unless otherwise specified:

- **Sensitivity to Analysis Set**

[redacted]

- **Kaplan-Meier Analysis**

[redacted]

- **Best-case Scenario**

[redacted]

- **Worst-case Scenario**

[redacted]

- **Tipping Point Analysis**

[redacted]

8.7 Subgroup Analyses

In order to provide additional characterization and interpretation of the primary effectiveness and safety outcomes, the below specified subgroup analyses will be performed in the Pivotal main phase. [redacted]

- **Baseline Characteristics:**
  - Age group: <65 vs. ≥65 years
  - CHA_2DS_2-VASC Score: ≤2 vs. >2
  - Race

- **Sex:** [redacted]

[redacted]

- **Operator Experience:** [redacted]

8.8 Assessment of Site Homogeneity

There will be up to 40 US sites recruiting approximately 225 evaluable subjects in the Pivotal main phase of the study. Each site should enroll no more than 15% of the total enrollment to minimize the possibility that the study results are highly influenced by a few sites. In order to assess the assumption of clinical comparability and justify pooling of the primary outcome data, homogeneity across individual sites for the primary safety and effectiveness endpoints will be examined both descriptively and formally for subjects in the Pivotal main phase.

[redacted]

[redacted]

8.9 **Exploratory Analyses**

[redacted]

8.10 **Handling of Missing Data**

Missing data will be queried for reasons and handled on an individual basis.

- **Primary Safety Endpoint:** [redacted]

- **Primary Effectiveness Endpoint:** [redacted]

8.11 Adjustments for Multiplicity

For the Pivotal main phase, the Type I error for each of the primary endpoints is controlled at a one-sided 2.5% level. The secondary endpoint will only be tested if the primary endpoints are met. The Family-wise error rate for the primary and secondary hypothesis tests will be controlled at a level of 2.5% by using this gatekeeping strategy. [redacted]

8.12 Analyses of Secondary Endpoints

Baseline AFEQT scores and changes from baseline at each follow-up timepoint the questionnaire is administered will be summarized descriptively in the Pilot SA, Pivotal main phase mITT and PP, and the Pivotal Roll-In analysis sets for the following five scores. [redacted]

If both primary endpoints are met, then hypothesis testing will be performed in the Pivotal main phase PP analysis set. A paired t-test at an alpha level of 2.5% will be used to test the mean change of overall AFEQT scores between baseline and 12 months post ablation procedure. If the mean change of the overall AFEQT score is greater than 0 and the statistical test p-value is ≤0.025, then the null hypothesis will be rejected in favor of the alternative hypothesis of AFEQT improvement.

8.13 Additional Endpoint Analyses

No formal statistical hypotheses will be formulated or performed for the additional endpoints. Descriptive statistics will be provided on all additional endpoints in the analysis sets specified below.

8.13.1 Additional Safety Endpoints

The additional safety endpoints will be summarized descriptively as the total number of events, the number of subjects with events, and the percentage of subjects with events and will be conducted in the Pilot SA, Pivotal main study SA, and Pivotal Roll-In analysis sets.

8.13.2 Additional Effectiveness Endpoints

The additional effectiveness endpoints will be summarized descriptively as described below and will be conducted in the Pilot SA, Pivotal main study mITT and PP, and Pivotal Roll-In analysis sets.

- **Acute procedural success**: The number and percentage of subjects and clinically relevant targeted PVs with acute procedural success will be presented.

- **Acute reconnection**: The number and percentage subjects and clinically relevant targeted PVs where acute reconnection was identified by adenosine/isoproterenol challenge will be presented:

[redacted]

- **FPI:** The number and percentage of subjects and clinically relevant targeted PVs with achievement of entrance block after first encirclement evaluated prior to the adenosine challenge:

[redacted]

- **Touch-up by NSC**: The number and percentage of subjects and clinically relevant targeted PVs ablated by a NSC to achieve PVI:

[redacted]

- **Repeat ablation procedure:**
  - **Occurrence of repeat procedures:** Kaplan-Meier estimates and plots will be used to characterize the time to the first repeat ablation procedure for AF/AT/AFL of unknown origin. The proportion of subjects who are free from repeat ablation for AF/AT/AFL of unknown origin at each monthly timepoint post index procedure will be presented.

    [redacted]

  - **PV reconnection:** The number and percentage of subjects and PVs and at the repeat procedure where PV reconnection was observed:

    [redacted]

[redacted]

- **Freedom from documented (symptomatic and asymptomatic) atrial tachyarrhythmia off Class I/III AAD:** Kaplan-Meier estimates and plots will be used to characterize the time to first documented (symptomatic and asymptomatic) atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365). Taking any Class I/III AAD for AF/AT/AFL of unknown origin during the evaluation period will also be deemed a failure. The proportion of subjects who are free from failure at each monthly time point post blanking will be presented.

- **12 Month Single Procedure Treatment Success:** Kaplan-Meier estimates and plots will be used to characterize the time to first documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365) following a single index ablation procedure with all other failure modes included. The proportion of subjects who are free from failure at each monthly time point post blanking will be presented.

- **Clinical Success:** Kaplan-Meier estimates and plots will be used to characterize the time to first documented symptomatic atrial tachyarrhythmia episodes based on electrocardiographic data (≥30 seconds on ECG or sponsor provided CEM or Holter device) during the effectiveness evaluation period (Day 91-Day 365). The proportion of subjects who are free from failure at each monthly time point post blanking will be presented.

- **CCS-SAF:** Baseline CCS-SAF scores and the mean change from baseline at each follow-up timepoint the questionnaire is administered will be summarized descriptively. [redacted]

- **Reduction in CV Hospitalization:** Baseline and follow-up rates for the time intervals 0-6 months and >6-12 months will be summarized descriptively. [redacted]

[redacted]

- **Reduction in DCCV:** Baseline and follow-up rates for the time intervals 0-6 months and >6-12 months will be summarized descriptively. [redacted]

- **AAD Utilization by Timing:** Baseline and follow-up AAD usage will be summarized descriptively. [redacted] Separate summaries will be presented for all AADs and Class I/III AADs.

8.13.3 **Additional Procedural Data**

Additional procedural data will be summarized descriptively in the Pilot SA, Pivotal main study mITT and PP, and Pivotal Roll-In analysis sets.

9 Data Monitoring Committee (DMC)

A DMC will assess subjects' data for safety on regular intervals for both Pilot and Pivotal phase subjects and make recommendations on study adaptations as described in the DMC Charter. There will be no formal interim analysis (sample size analysis or early success analysis).

10 Reference(s)

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4. Wilson, J.T., et al., *Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin Scale.* Stroke, 2002. **33**(9): p. 2243-6.