Abbott	Statistical Analysis Plan Cover Page

NCT Number: NCT03882021
WAVE-MAP AF
High-Density Wave Mapping in Subjects with Atrial Fibrillation as a Predictor of Recurrence After a Single Ablation Procedure Using a PVI-Only Strategy
Date: 26-JUL-2019

Sponsor

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CRD_968

WAVE-MAP AF

High-Density Wave Mapping in Subjects with Atrial Fibrillation as a Predictor of Recurrence After a Single Ablation Procedure Using a PVI-Only Strategy

Statistical Analysis Plan (SAP)

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

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1. ACRONYMS AND ABBREVIATIONS

Acronym or Abbreviation	Complete Phrase or Definition
AAD	Antiarrhythmic Drug
AF or AFib	Atrial Fibrillation
AFL	Atrial Flutter
AT	Atrial Tachycardia
HD	High Density
LA	Left Atrium
LAA	Left Atrial Appendage
LVEF	Left Ventricular Ejection Fraction
NYHA	New York Heart Association
PVI	Pulmonary Vein Isolation
SAP	Statistical Analysis Plan

2. SYNOPSIS OF STUDY DESIGN

2.1 Purpose of the Statistical Analysis Plan

This statistical analysis plan (SAP) is intended to provide a detailed and comprehensive description of the planned analysis to be used for CRD 968 WAVE-MAP AF clinical investigation. [redacted]

2.2 Clinical Investigation Objectives

The primary objective of this study is to characterize low-voltage substrate, as identified via HD Wave mapping in sinus rhythm, and identify association with 12-month recurrence rates after a single pulmonary vein isolation (PVI) with a contact force ablation catheter. Other objectives of this study include:

- Analyze additional maps and data collected with GRID and associations with 12-month recurrence rates, such as
  - Voltage maps using different configurations recreated post procedure
  - Voltage maps using different thresholds for low-voltage
    Fractionation maps
- [redacted]

2.3 Clinical Investigation Design

This is a post-market, single-arm, multi-center, prospective interventional study of the Advisor™ HD Grid Mapping Catheter, Sensor Enabled™. [redacted] Scheduled visits and data collection will occur at baseline, index procedure, 3, 6 and 12-month follow up visits. Subjects will be exited from the trial at the conclusion of their 12-month follow-up visit. [redacted]

2.4 Endpoint and Additional Data

2.4.1 Primary Endpoint

The primary outcome is one-year success, defined as freedom from AF/AFL/AT after removal from antiarrhythmic drug therapy as assessed from the end of the 3-month blanking period to 12 months following a single ablation procedure.

Occurrence of isthmus-dependent atrial flutter, if confirmed during electrophysiology testing, should not be considered a failure for this outcome. This endpoint is based on the recommendations from the 2017 HRS consensus paper.[1]

[redacted]

2.4.2 Additional Data

Additional data to be collected will include the following:

- Acute procedural success, defined as electrical isolation of all pulmonary veins.
- Success post blanking period through 12 months using different definitions, including:
    - Freedom from symptomatic AF/AFL/AT after removal from AAD therapy
    - Single procedure clinical success defined as freedom from symptomatic AF/AFL/AT without a new or increased dose of class I or III AAD
    - Freedom from AF/AFL/AT
    - Freedom from AF
- Data from EnSite maps using both HD Wave and Standard mapping modes in both sinus rhythm and AF including but not limited to:
    - Left atrial area using different boundaries (e.g. with and without LAA, etc.)
    - Low voltage area and proportion of left atria with low voltage using different cutoffs for voltage
- Rates of recurrence not due to PVI gap for subjects with repeat electrophysiology studies
- LA volume and diameter
- Adverse events including any device-, procedure-, or death-related events
- Other baseline characteristics including but not limited to:
    - Time with AF
    - Type of AF
    - Age
    - Sex
    - BMI
    - General medical history
    - Cardiovascular history
    - Arrhythmia history
    - NYHA classification
    - LVEF
    - Presence of pacemaker
    - Left ventricular hypertrophy
    - History of heart failure
- Procedural characteristics, including but not limited to:
    - Power, temperature, and contact force

[redacted]

- Procedure time
- Mapping time
- Cardioversions (if applicable)
- Anesthesia
- Fluoroscopy time

3. ANALYSIS CONSIDERATIONS

3.1 Statistical Methods

Depending on the type of data, appropriate statistics and analyses described in the section below will be used.

3.1.1 Descriptive Statistics for Continuous Variables

Continuous (CONT) variables will be summarized with the numbers of observations, means, standard deviations, quartiles, minimums, maximums, and 95% confidence intervals for the means. When comparing HD Wave with standard mapping modes, differences in each measurement between the two modes will be summarized with the mean of the differences and its 95% confidence interval (Appendix A).

3.1.2 Descriptive Statistics for Categorical Variables

Categorical (CAT) variables will be summarized with subject counts and percentages/rates with exact 95% Clopper-Pearson confidence intervals (Appendix B).

3.1.3 Survival Analyses

Survival (SURV) analysis will be conducted to analyze time-to-event variables. Subjects without events will be censored at their last known event-free time point. Subjects withdrawn or otherwise lost-to-follow-up during the follow-up period will be censored at their last known visit. Survival data will be presented using the Kaplan-Meier product limit method. Number of subjects at risk, number of censored subjects, number of events, event free survival rate and standard error of the survival rate at each follow-up time point will be presented in a summary table.

3.1.4 Logistic Regression

Logistic regression (LOGIT) analysis will be used [redacted]

[redacted]

3.2 Planned Analyses

3.2.1 Analysis Populations

3.2.1.1 Enrolled Population (ENR)

[redacted]

3.2.1.2 Per-Treatment Evaluable Population (PTE)

[redacted]

3.2.2 Sample Size Calculation

[redacted]

3.2.3 Timing of Analysis

Data analyses will be performed at the completion of the 12-month follow-up period for all subjects or as desired by Sponsor. In addition, study progress and data may be summarized and reported as needed.

3.2.4 Endpoint and Variables for Analysis

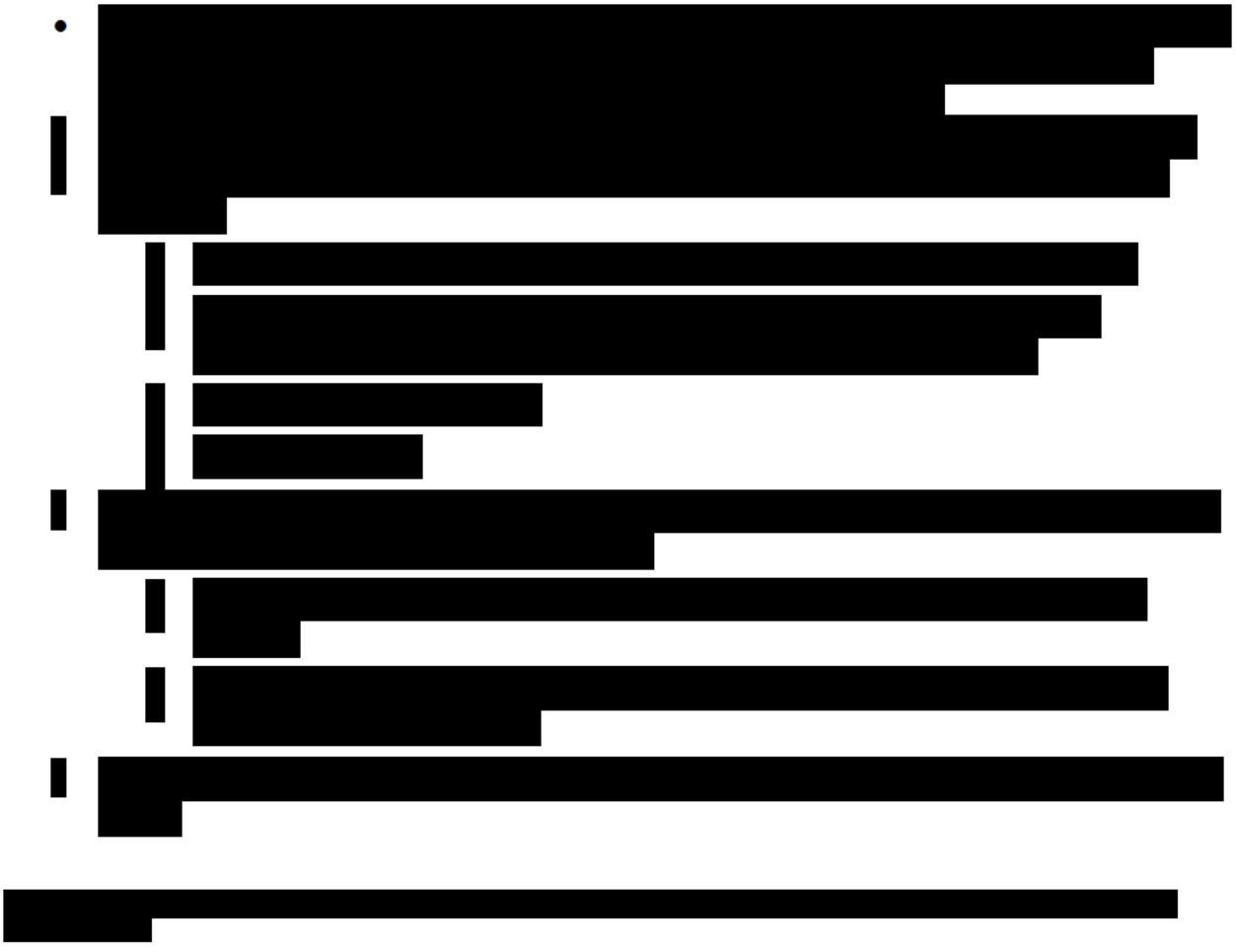
The following lists describe the variables and analysis methods that will be analyzed in the ENR population:

- LA volume and diameter (CONT)
- Adverse events including any device-, procedure-, or death-related events (CAT)

[redacted]

- Other baseline characteristics including but not limited to:
  - Time with AF (CONT)
  - Type of AF (CAT)
  - Age (CONT)
  - Sex (CAT)
  - BMI (CONT)
  - General medical history (CAT)
  - Cardiovascular history (CAT)
  - Arrhythmia history (CAT)
  - NYHA classification (CAT)
  - LVEF (CONT)
  - Presence of pacemaker (CAT)
  - Left ventricular hypertrophy (CAT)
  - History of heart failure (CAT)

The following lists describe the analysis methods for the primary endpoint and additional evaluations that will be analyzed in the PTE population:



3.3 Special Analysis Issues

3.3.1 Handling of Missing Data

Every effort will be made to collect all required data. All data available for the endpoints specified among the analysis population will be used. Missing data will not be imputed. Kaplan-Meier analysis will censor subjects withdrawn or otherwise lost-to-follow-up at last known visit.

3.3.2 Poolability Analysis

No poolability analysis will be performed.

3.3.3 Multiplicity

No hypothesis testing will be performed; therefore, no adjustments will be made for multiplicity in the endpoint analyses.

3.4 Documentation and Other Considerations

Analyses will be performed using SAS® for Windows, version 9.4 or R for Windows, version 3.5.3 or higher.

4. REFERENCES

1. [redacted]

5. APPENDICES

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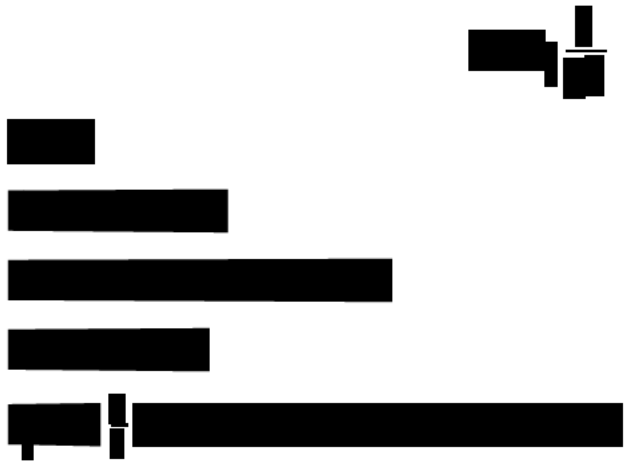

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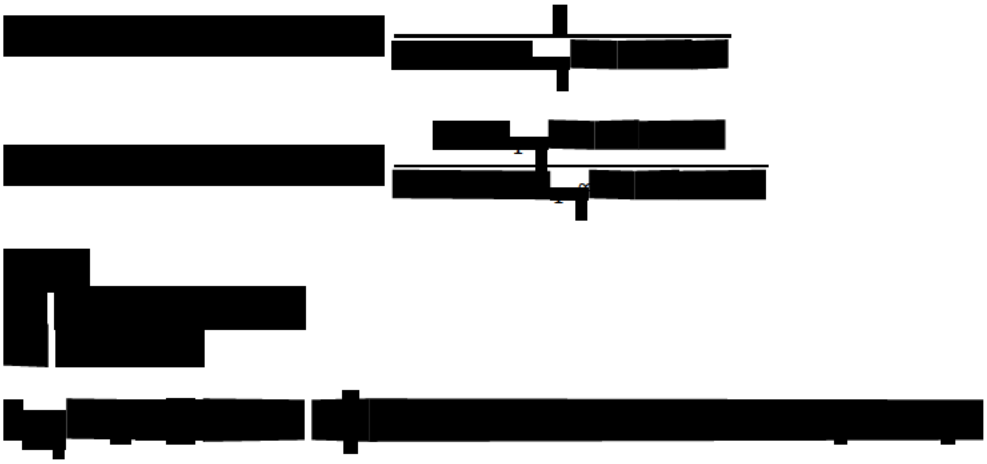

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