Abbott	Statistical Analysis Plan Cover Page

NCT Number: NCT03719040
CRD955 PP Registry
Physiologic Pacing Registry
Study Document No: < ABT-CIP-10270>
Version A
Date: 5-April-2021

Sponsor	Abbott 15900 Valley View Ct. Sylmar, CA 91342 USA

Protocol [redacted]
CRD955 PP Registry

Physiologic Pacing Registry

Statistical Analysis Plan (SAP)

[redacted]

[redacted]

[redacted]

TABLE OF CONTENTS

1.0 SYNOPSIS OF STUDY DESIGN

1.1 Purpose of the Statistical Analysis Plan

This statistical analysis plan (SAP) is to provide a detailed and comprehensive description of the planned methodology and analysis to be used in the Physiologic Pacing (PP) registry study. This plan is based on the version C of Clinical Investigational Plan (CIP).

1.2 Clinical Investigation Objectives

The PP Registry will characterize the implant and follow-up measures associated with physiologic pacing device implants. The registry will also compare the implant and follow-up characteristics for these device implants with and without utilizing the EnSite Cardiac Mapping System, based on the sites' routine care. Data on all tools used as chosen by the physicians as part of their standard practice will be collected. Abbott will collect data based on the characteristics at implant and follow-up.

1.3 Clinical Investigation Design

The PP Registry is a prospective, observational, multi-center registry designed to characterize device data at implant and follow-up in patients with a permanent physiologic pacing lead and an Abbott pacemaker, defibrillator, or CRT-P/D. The devices selected for use will be at the discretion of the implanting physician.

The registry will enroll up to 1,000 subjects from up to 75 participating centers worldwide.

The total duration of the registry is expected to be 4 years, including enrollment and data collection from all subjects.

1.4 Endpoints

The PP Registry will collect data on the following measures as recommended by the His Bundle Pacing Collaborative Working group[1] to characterize the workflow associated with physiologic pacing device implants and follow-up, and to quantify the clinical utility of mapping the cardiac structures prior to physiologic pacing device implants according to sites' routine care. Implant and follow-up characteristics will be compared with and without utilizing the EnSite Cardiac Mapping System during device implants.

Implant Characteristics:

- Fluoroscopy time and radiation dose

- Overall procedure time[redacted]
- Implant procedure time[redacted]
- All implant tools used
- Implant-related workflow
  [redacted]
- Final implanted hardware
- Final post-procedure device programming
  [redacted]
- Procedure- and device-related adverse events and device deficiencies
- Implant success[redacted]
- All types of physiologic pacing capture observed such as selective and non-selective
- Physiologic pacing capture and sensing thresholds
- Pacing output necessary to correct bundle branch block using 12-lead ECG (if applicable)
- QRS duration at baseline and following implant using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing

Follow-up Characteristics:

- Follow-up related workflow
- Physiologic pacing capture and sensing thresholds
- For His placement only: Measured H wave using device IEGM
- Measured R wave using device IEGMs through the lead implanted for physiologic pacing
- Presenting PR interval and QRS duration using 12-lead ECG
- QRS duration for all types of physiologic pacing captures observed using 12-lead ECG

- Incidence of increase in capture threshold of > 1V in leads implanted for physiologic pacing or RV pacing leads
- Far-field atrial oversensing and ventricular oversensing and/or any interventions – including programming – required to address these issues
- NYHA Classification
- LVEF, LVEDV, LVESV (if available)
- Tricuspid and mitral regurgitation severity by echocardiogram (if available)
- Device estimated battery longevity via device session records
- Frequency/burden of detected atrial and ventricular arrhythmias via device session records
- Procedure and device-related adverse events

2.0 ANALYSIS CONSIDERATIONS

2.1 Analysis Populations

2.1.1 Enrollment Population

The enrollment population includes all subjects enrolled (upon providing written informed consent) in the registry.

2.1.2 Implanted Population

The implanted population includes subjects enrolled in the registry, implanted with Abbott device, and have an active (programmed on) lead implanted for physiologic pacing post implant.

2.2 Statistical Methods

Descriptive analysis will be performed to summarize baseline, procedural, safety and effectiveness endpoints and clinical safety event data. Depending on the type of data (e.g. continuous or categorical), statistical methods described in this section below will be used.

2.2.1 Descriptive Statistics for Continuous Variables

For continuous variables (e.g., age, blood pressure, 12-lead ECG, etc.), results will be summarized with the numbers of observations, means, and standard deviations, and in addition, with medians, quartiles, minimums, maximums. The 95% confidence intervals may also be provided for the means, when specified.

2.2.2 Descriptive Statistics for Categorical Variables

For categorical variables (e.g. sex, NYHA class, etc.), results will be summarized with subject counts and percentages/rates. The exact 95% Clopper-Pearson[2] confidence intervals may also be provided when specified.

2.2.3 Survival Analyses

Survival analysis will be conducted to analyze time-to-event variables. Subjects without events will be censored at their last known event-free time point. Survival curves will be constructed using Kaplan-Meier estimates.

2.3 Endpoint Analysis

2.3.1 Implant Characteristics

There is no pre-specified hypothesis testing for the implant characteristics. All the implant characteristics will be summarized descriptively.

2.3.2 Follow-up Characteristics

There is no pre-specified hypothesis testing for the follow-up characteristics. All the follow-up characteristics will be summarized descriptively at 1-month and 6-month.

2.4 Sample Size Calculations

There is no hypothesis testing in this registry. Therefore, no formal sample size calculation has been performed.

2.5 [redacted]

[redacted]

2.6 [redacted]

[redacted]

2.7 Subgroups for Analysis

Major implant characteristics will be summarized by subgroups, which include but are not limited to the following:

- Ensite Mapping system used to identify His signal [redacted]
- Physiologic pacing mode [redacted]

[redacted]

2.8 Handling of Missing Data

All analyses will be based on available data with missing data excluded, unless otherwise stated.

3.0 DESCRIPTIVE ENDPOINTS AND ADDITIONAL DATA

3.1 Baseline and Demographic Characteristics

The baseline and demographic variables will be summarized for the subjects enrolled: gender, age, ethnicity, race, echocardiogram measurements, NYHA class, and 12-lead ECG, etc.

3.2 Adverse Events

All of the adverse device effects, serious adverse device effects, UADEs, USADEs will be summarized for all subjects who enrolled in this trial in terms of the number of events and the percentage of subjects with events. Procedure and device related AEs will also be summarized.

3.3 Subject Early Termination

Subject early termination reasons including deaths, withdrew consent, lost-to-follow-up, unsuccessful implant/procedure, subject not moving forward with implant of a lead for physiologic pacing, etc. will be summarized.

3.4 Protocol Deviation

Protocol deviations will be summarized for subjects in whom a protocol deviation was reported.

4.0 DOCUMENTATION AND OHER CONSIDERATIONS

All analyses will be performed using SAS® for Windows, version 9.4 or higher.

5.0 ACRONYMS AND ABBREVIATIONS

Acronym or Abbreviation	Complete Phrase or Definition
AE	Adverse Event
CIP	Clinical Investigation Plan
CRF	Cardiac Resynchronization Therapy
CRT-D	Cardiac Resynchronization Therapy Defibrillator
CRT-P	Cardiac Resynchronization Therapy Pacemaker
ECG	Electrocardiogram
HBP	His Bundle Pacing
IEGM	Intracardiac Electrogram
LBBP	Left Bundle Branch Pacing
LV	Left Ventricular
LVEF	Left Ventricular Ejection Fraction
LVESV	Left Ventricular End Systolic Volume
LVEDV	Left Ventricular End Diastolic Volume
NYHA	New York Heart Association
SAE	Serious Adverse Event
PP	Physiologic Pacing
SAP	Statically Analysis Plan

6.0 REFERENCES

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2. Clopper C. J., Pearson E. S., “The Use of the Confidence or Fiducial Limits Illustrated in the Case of the Binomial.” *Biometrika*, 1934, 26, 404-413.

3. Vijayaraman P, et al. Permanent His bundle pacing: Recommendations From a Multicenter His Bundle Pacing Collaborative Working Group for standardization of definitions, implant measurements, and follow-up. Heart Rhythm 2018;15:460-468.

4. SAS/STAT® 9.4 User’s Guide, Second Edition, SAS Institute Inc., Cary, NC, 2019.

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