Title: NUVISION NAV Statistical Analysis Plan

Statistical Analysis Plan (SAP)

Clinical Evaluation of Intracardiac Ultrasound
with the NUVISION™ NAV Ultrasound Catheter.
"NUVISION NAV Study"
(BWI202104)
Protocol Version: 2.0

SAP Revision: 1.0
SAP Revision Date: 08APR2024

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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
1.0	08/04/2024	Original document

List of Acronyms and Abbreviations

Acronym/Abbreviation	Expanded Term
AE	Adverse Event
AT	Atrial Tachycardia
CV	Cardiovascular
ICF	Informed Consent Form
LA	Left Atrium
LAAO	Left Atrial Appendage Occlusion
LV	Left Ventricle
NYHA	New York Heart Association
PAF	Paroxysmal Atrial Fibrillation
PP	Per Protocol
PsAF	Persistent Atrial Fibrillation
PVC	Premature Ventricular Complex
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
TTE	Transthoracic Echocardiography
VT	Ventricular Tachycardia

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1 Study Design

This study is a prospective, single arm, non-randomized, open-label, multi-center study. Up to 30 subjects will be enrolled.

Subjects meeting the inclusion / exclusion criteria and who sign the informed consent form (ICF) will be enrolled in this study. The clinical investigation is targeting approximately 4 sites in Europe and Israel.

This study will serve to characterize the performance and safety of using the investigational catheter in procedures for subjects in up to five different subgroups (scar-related AT, PsAF, PAF, VT and PVC). Subjects will be treated per investigator's standard of care and followed until 7 days post-procedure.

The primary objective of this study is to assess the performance and safety of using the investigational catheter.

A secondary objective is to gather physician assessment of deployment, maneuverability, navigational features and imaging quality acquired with the investigational catheter.

2 Treatment Assignment

This is a single arm clinical study and all enrolled patients will use the investigational NUVISION™ NAV Ultrasound Catheter (D-1426-01-SI), which is a sterile, single use, disposable, diagnostic ultrasound imaging catheter designed for intracardiac use. It is built around the core design and technology of the existing NUVISION™ Ultrasound Catheter, 10 Fr (D-1423-01-S).

3 Randomization and Blinding Procedures

This is a non-randomized, open-label study.

4 Interval Windows

See Section 14.3 of the study protocol.

5 Levels of Significance

All data will be summarized by descriptive analyses. No formal hypothesis testing will be performed. All confidence intervals will use the two-sided 95% confidence level unless otherwise stated.

6 Analysis Sets

Safety Analysis Set: The Safety Analysis Set will consist of all enrolled subjects who have undergone insertion of the NUVISION™ NAV Ultrasound catheter.

Per Protocol (PP) Analysis Set: The PP Analysis Set will include all enrolled subjects who met the study eligibility criteria and in whom assessments were performed with the NUVISION™ NAV Ultrasound catheter.

7 Sample Size Justification

A sample size of 30 subjects will be enrolled to characterize the performance and safety of the Investigational catheter.

The sample size is selected based on previous experience with similar design in first in human assessments of multi-electrode mapping catheters. This study is meant to characterize the catheter's ability to perform safely in various types of arrhythmias. No clinical claims of effectiveness or patient outcomes will be made from this study.

8 Statistical Analysis Methods

8.1 **General Conventions**

SAS® version 9.4 or higher will be used for all analysis. Standard descriptive summaries for continuous data include the number of observations with data, number of observations with missing data, mean, standard deviation, median, minimum, and maximum values. For categorical data, the count and percentage will be provided. Percentages will be based on the number of subjects without missing data.

8.2 **Disposition of Study Subjects**

Subject disposition will be summarized and listed for the subject categories defined in protocol section 10.3 for all subjects. Subject disposition will be summarized using categorical summaries. The number and percent of patients who are enrolled in the study, fail inclusion/exclusion criteria, are included in the safety, and per-protocol analysis sets, complete the study, and prematurely discontinue from the study will be presented. Patients who are prematurely discontinued will be summarized by primary reason for discontinuation.

8.3 **Demographic and Baseline Characteristics**

Demographic variables will include age and sex. Baseline characteristics will include the primary study arrhythmia/procedure and the number of previous ablation procedures. All demographic and baseline characteristics will be summarized using categorical and continuous summaries, as appropriate, for the Safety Analysis Set. A listing of subject demographic and baseline characteristics will be generated.

Medical history will be presented using the Safety Analysis Set.

Cardiovascular (CV) and Thromboembolic/Cerebrovascular medical history will be collected and summarized using categorical summaries. Each subject will be

counted once under each type of CV and/or thromboembolic/cerebrovascular medical history they have experienced.

The number of subjects with TTE performed and those with pericardial effusion will be presented using categorical summaries. The left ventricle ejection fraction and the maximum dimension of pericardial effusion will be presented in continuous summaries.

The number of subjects with an exam performed to assess the presence of thrombus and whether a thrombus is present will be summarized.

Other medical history, including NYHA class, occurrence of diabetes, and history of bleeding will be summarized similarly.

8.4 Endpoint(s) *and Associated Hypotheses*

8.4.1 Primary Endpoint(s)

Safety: Occurrence of serious adverse events within 7 days of index procedure related to the NUVISION™ NAV Ultrasound Catheter

Performance: Completion of imaging required for the study procedure with the NUVISION™ NAV Ultrasound Catheter without resort to a non-study ultrasound device

8.4.2 Secondary Endpoints

Physician assessment of deployment, maneuverability, navigational features and imaging quality acquired with the NUVISION™ NAV Ultrasound Catheter during the study procedures

Occurrence of all other serious adverse events within 7 days of index procedure (not related to the NUVISION™ NAV Ultrasound Catheter)

Occurrence of non-serious adverse events within 7 days of index procedure related to the NUVISION™ NAV Ultrasound Catheter

8.4.3 Additional Endpoints

Additional Procedural data, including:
- Anatomical structures assessed
- Whether imaging for Left Atrium (LA) and Left Ventricle (LV) volume measurements was done
- Total fluoroscopy time
- Total procedure duration

Additional safety data: All non-serious AEs not related to the investigational catheter

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

Primary Safety Endpoint is defined as the occurrence of serious adverse events related to the Investigational catheter within 7 days of index procedure. An SAE will be counted as related to the investigational catheter if the relationship to a study catheter is anything other than 'Not Related'.

The number of subjects with SAEs related to the investigational catheter will be summarized in the Safety Analysis Set overall and per procedure type (atrial ablation/ventricular ablation) by System Organ Class and Preferred Term and level of relationship. All tables will present summaries both by subject and by event. If a subject has multiple occurrences of an event within a level of summarization, then for the by-subject summaries only a single occurrence will be counted at each level of summarization at the highest level of severity/relationship; for the by-event summary all events will be counted.

All investigational catheter related SAEs will be listed by System Organ Class and Preferred Term, severity, causality (defined as possible, probable or having a causal relationship to the device and/or procedure), anticipation and outcome.

Primary Performance Endpoint is defined as the completion of imaging required for the study procedure with the NUVISION™ NAV Ultrasound Catheter without resort to non-study ultrasound device(s).

The number of subjects who successfully completed the procedure without resort to a non-study ultrasound device will be summarized overall and per procedure type (atrial ablation/ventricular ablation) for the PP Analysis Set.

A listing of the primary performance endpoint will be provided.

8.6 **Analysis of Secondary Endpoint(s)**

Secondary Safety Endpoints will be analyzed using the Safety Analysis Set:

− All Serious Adverse Events, excluding investigational catheter related SAE, during the 7-day follow-up period.

− All non-serious Adverse Events related to the investigational catheter during the 7-day follow-up period

The number of subjects experiencing serious adverse events excluding investigational catheter related SAE and the number of serious adverse events excluding investigational catheter related SAE will be summarized in the Safety Analysis Set overall and per procedure type (atrial ablation/ventricular ablation) using categorical summaries similar to the primary safety endpoint.

The number of subjects experiencing non-serious adverse events related to the investigational catheter and the number of non-serious adverse events related to the investigational catheter will be summarized in the Safety Analysis Set overall and per

procedure type (atrial ablation/ventricular ablation) using categorical summaries similar to the primary safety endpoint.

All SAEs excluding investigational catheter related SAE and all non-serious AEs related to investigational catheter will be listed by System Organ Class and Preferred Term, severity, causality (defined as possible, probable or having a causal relationship to the device and/or procedure), anticipation and outcome.

A listing of device deficiencies including the category and timing of the device deficiency will also be provided. Each deficiency will indicate whether it results in an adverse event.

Physician feedback on deployment, maneuverability, navigational features and imaging quality acquired with the investigational catheter will be analyzed using the PP Analysis Set. A post-procedure survey will be administered. Each question/sub-question will be answered by the physician using a Likert scale of 1 to 7 (1=poor and 7=excellent) and will be summarized. The summary results of each question will be presented overall and per procedure type (atrial ablation/ventricular ablation) using continuous summaries. A by subject listing including all feedback results will be provided.

8.7 **Analysis of Additional Endpoint(s)**

Additional Procedural Data will be analyzed overall and per procedure type (atrial ablation/ventricular ablation) using the PP Analysis Set and include the following parameters:
- Whether Imaging for Left Atrium (LA) and Left Ventricle (LV) volume measurements was done;
- Total fluoroscopy time;
- Total duration of the procedure.

For each of the above procedural data, the denominator will be the number of subjects where assessments with the study device are performed. Listings will be provided.

Additional safety data, e.g., all non-serious AEs not related to the investigational catheter will be listed by System Organ Class and Preferred Term, severity, causality (defined as possible, probable or having a causal relationship to the device and/or procedure), anticipation and outcome.

8.8 **Handling of Missing Data**

No missing data will be imputed in this study. All analyses will be performed using observed data.

8.9 **Subgroup Analysis**

Primary and secondary safety endpoints and primary performance endpoint will be further summarized descriptively in the following subgroups:

1. Scar-related Atrial Tachycardia
2. Persistent Atrial Fibrillation (PsAF)
3. Paroxysmal Atrial Fibrillation (PAF)
4. Ventricular Tachycardia (VT)
5. Premature Ventricular Complex (PVC)

9 Appendix: Tables, Listings and Graphs Shells

Provide, or reference the document that contains the tables, listings and graphs shells. May be replaced with other document (i.e. simulation reports), as appropriate.

10 Reference(s)

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