Statistical Analysis Plan (SAP)

Radial AccEss for Navigation to your Chosen Lesion for Peripheral Vascular Intervention: (REACH PVI)

[redacted]

[redacted]

NCT 03943160

19-November-2019

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[redacted]	[redacted]		

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1. INTRODUCTION

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analysis of clinical study data collected under study protocol [redacted], Radial accEss for nAvigation to your CHosen lesion for Peripheral Vascular Intervention (REACH PVI). This SAP should be read in conjunction with the study protocol and Case Report Forms (CRF). This version of the plan has been developed with respect to REACH PVI study protocol [redacted] Any changes to this protocol or the CRFs may necessitate updates to the SAP.

2. STUDY OBJECTIVE

The objective of this study is to evaluate acute clinical results of orbital atherectomy (OA) via radial artery access, including complication rates and cost effectiveness.

2.1 Primary Outcome Measure: Procedural Success

Procedural success is defined as successful completion of OA treatment of the target lesion via transradial access (TRA) without serious transradial access related events.

2.2 Secondary Outcome Measure: Treatment Success

Treatment success is defined as <50% residual stenosis post-procedure and without significant angiographic complications without stent placement, or <30% residual stenosis post-procedure and without significant angiographic complications with stent placement.

[redacted]

3. STUDY DESIGN

This prospective, observational, single-arm, multi-center post-market clinical study is designed to prospectively evaluate acute clinical outcomes of OA via TRA for treatment of peripheral artery disease (PAD) in lower extremities

3.1 Enrollment

This study will enroll approximately (50) subjects at up to ten (10) active sites in the United States (US) who have signed an IRB-approved informed consent, have met all inclusion criteria and none of the exclusion criteria, and the ViperWire has been inserted into the body. For a full list of criteria for subject eligibility, refer to [redacted], section 9.0. Subjects found to not meet index inclusion criteria or to meet index exclusion criteria will be considered consented screen failures.

[redacted]

3.2 Duration

The duration of this study is expected to be approximately eight (8) months. Subjects will be followed post-procedure through the first standard of care follow-up visit (7-45 days post procedure) only.

3.3 Sample Size

As a hypothesis generating study, this study is not powered.

[redacted]

4. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5. DATA ANALYSIS SETS

The Primary Analysis will be based on the Intent to Treat (ITT) analysis set, unless otherwise noted. The following analysis sets are specified for REACH PVI.

5.1 Intent to Treat (ITT) Analysis Set

The ITT analysis set will include all enrolled subjects who have been enrolled regardless of deviations from the protocol.

[redacted]

6. DATA ANALYSIS METHODOLOGY & CONVENTIONS

The primary analysis of REACH PVI subjects will be based on archived clinical data and the ITT analysis set unless otherwise noted.

Statistical analyses will be performed using SAS® software (SAS Institute Inc., SAS Campus Drive, Cary, NC 27513, USA). In the event an analysis is required that is better suited for a statistical package other than SAS (e.g., SPSS, R), the other package may be used.

6.1 Timing of Analysis

Analyses of all primary and secondary outcome measures will be performed after all ITT subjects have a completed end of study (EOS) CRF, all queries have been resolved, and the physician has signed all subject CRFs.

6.2 Analysis Conventions

This section details the general conventions to be used for data analysis. Departures from these general conventions may be given in the specific detailed sections of this SAP. When this occurs, the rules set forth in the specific section take precedence over the general conventions. Departures from the plans laid out in this document will be explained and justified with appropriate scientific, clinical and/or statistical justification.

- Data will be summarized for the ITT analysis set unless otherwise noted
- Continuous variables will be summarized using mean, standard deviation (SD), median, quartiles, minimum, and maximum and the number of subjects with non-missing data
- Categorical and discrete variables will be summarized by the number and percent of responses in each category and rounded to a single decimal point
- Unless otherwise specified missing data will be excluded from the denominator
- Confidence intervals will use an alpha level of 0.05
- If required for an analysis, partial dates will be completed by imputing the date using the most conservative approach for that specific date
- All listings will be sorted for presentation in order of site, subject number, and the date-time of the procedure or event (when applicable)
- Outcomes examining the standard-of-care (SOC) follow-up visit will be presented as binomial outcomes with the denominator equal to the number of patients with the SOC follow-up visit.

[redacted]

[redacted]

[redacted]

6.4 Analysis Windows

Assessments will be made at baseline (≤ 30 days prior to procedure), pre-procedure (≤ 24 hours prior to procedure), during the procedure, and post-procedure/discharge. A standard-of-care in-office follow-up visit is scheduled at 7-45 days post-procedure. All intervals will be calculated in days (e.g., 1-month will be calculated as 30 days).

7. REQUIRED DATA ANALYSES

The following analyses will be performed on the ITT population unless otherwise noted. Analyses will occur on the target lesion, defined as the stenotic segment appropriate for treatment with the Orbital Atherectomy System study device(s) via transradial access. The target lesion will be:

- The first lesion with Orbital Atherectomy attempted OR
- The first lesion with Orbital Atherectomy attempted after other successful peripheral intervention(s) without the occurrence of a reportable adverse event.

The study will be limited to one (1) target lesion per enrolled subject.

7.1 Subject Disposition

Subject disposition data will be provided for:

- The number of subjects enrolled at each site [redacted]
- Compliance to the follow-up visit schedule
- The number and percentage of subjects by discontinuation reason

7.2 Baseline Summary

Baseline characteristics such as subject demographics, clinical history, risk factors, and history of peripheral intervention will be summarized using descriptive statistics.

[redacted]

7.4 Primary Outcome Measure Analysis

Analysis of the primary outcome measure of Procedural Success will be assessed post-procedure on the ITT analysis set. Procedural Success is comprised of:

- Successful completion of OA treatment via transradial access determined by use of the device within the target lesion
- The presence of no serious transradial access related events. TRA related events include:
    - Serious TRA site bleeding (BARC Type 2-5)
    - Serious TRA site hematoma
    - Serious radial artery spasm
    - Serious hand ischemia
    - Stroke
    - Transient Ischemic Attack (TIA)
    - Serious nerve damage
    - Perforation
    - TRA site pseudoaneurysm

Procedural Success is considered successful for a subject if all criteria are met.

[redacted]

7.8 Adverse Event (AE) Rates

Adverse event rates will be assessed on the ITT analysis set. All reportable adverse events specified in the protocol will be included in the analysis. Adverse events are collected starting at enrollment through subject exit from the study. AEs will be summarized by AE term and overall for number and percent of subjects experiencing each event, and number of events. AEs will also be summarized by AE category.

Adverse events summaries will be provided through study exit in the following groups:

- Serious Adverse Event (SAE): Any AE that meets the protocol definition of serious

[redacted]

Any events for which the determination of seriousness and/or relatedness to the device cannot be determined will count as serious and/or related for the purposes of this analysis.

[redacted]

8. OTHER ANALYSES

No further analyses are planned outside those outlined in **Section 7 Required Data Analyses**. Any ad hoc analyses will follow the guidelines outlined in this document.