Statistical Analysis Plan

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NCT02561299

Project Title: OPTIMIZE BTK:
Orbital vessel PreparaTIon to MaximIZe dcb Efficacy in calcified below the knee (BTK) lesions- A pilot study

Sponsor:

Cardiovascular Systems, Inc. (CSI)

15 MAR 2019

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[redacted]	[redacted]	[redacted]	[redacted]

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2 INTRODUCTION

This statistical analysis plan (SAP) describes the statistical methods to be used during the reporting and analysis of data collected for the CSI OPTIMIZE [redacted] clinical study. This SAP should be read in conjunction with the study protocol and electronic Case Report Forms (eCRF). This version of the plan has been developed with respect to the OPTIMIZE BTK protocol revision C dated 20-May-2016. Any changes to the protocol or eCRF may necessitate updates to the SAP.

3 STUDY DESIGN

This prospective, randomized, multi-center, post-market pilot study includes subjects with calcified lesions of the distal popliteal (POP), anterior tibial (AT), posterior tibial (PT), tibial peroneal trunk (TPT) or peroneal (PR) arteries with ≥ 70% diameter stenosis (DS) by angiography.

Subjects will be randomized 1:1 to orbital atherectomy (OA) with adjunctive Drug Coated Balloon (DCB) angioplasty versus DCB angioplasty alone.

[redacted]

3.1 Analysis Objectives

The primary objective is to prospectively evaluate acute and long term clinical results of OA with adjunctive DCB angioplasty versus DCB angioplasty alone for treatment of PAD in Below the Knee (BTK) lesions. See section 5.5 for the detailed outcome measures.

Study outcome measures will be analyzed and reported using descriptive statistics.

[redacted]

4 DATA SET SPECIFICATIONS

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

4.5 Endpoints Analysis Sets

4.5.1. Intent to Treat (ITT) Analysis Set

[redacted]

[redacted] The ITT analysis set will include all randomized patients in the groups to which they were randomly assigned, regardless of their adherence with the entry criteria, regardless of the treatment they actually received, and regardless of subsequent withdrawal from treatment or deviation from the protocol.

[redacted]

5 DATA ANALYSIS

The analysis of OPTIMIZE BTK clinical study subjects will be based on locked clinical data and the evaluable analysis set, unless otherwise noted.

All statistical analyses will be completed 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, this other package (e.g. R) will be used.

5.1 Timing of Analysis

Analysis of the study objectives will occur throughout the duration of the study as subjects reach the relevant time points specified in section 5.5.

5.2 Analysis Conventions

This section details the general conventions to be used for data analyses. 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 convention. Departures from the plans laid out in this document will be explained and justified with appropriate scientific, clinical, and/or statistical justification.

- No formal hypothesis tests will be performed. No multiple testing adjustments will be made.
- Data will be summarized by treatment group.
- Continuous variables will be summarized using means, standard deviations (SD) or standard errors (SE), medians, minimums, and maximums and the number of patients with non-missing data.
- Summary statistics for discrete variables will consist of the number and percent of responses in each category.
- 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).

5.3 Subject Disposition

Subject disposition will be presented by:

- The number of subjects who were enrolled
- [redacted]
- The number and percentage of subjects participating in each visit
- The number and percentage of subjects by discontinuation reason overall

5.4 Baseline Data Summary

Baseline data such as subject demographics, clinical history, risk factors, and pre-procedure lesion characteristics will be summarized using descriptive statistics by treatment arm.

5.5 Outcome Measures

The following outcomes measures have been defined in the OPTIMIZE BTK study protocol.

[redacted]

5.5.2. Patency of Target Lesion

Patency is determined from the max peak systolic velocity (mPSV) as assessed by Duplex Ultrasound (DUS) within the target lesion or if no mPSV of the lesion, the mPSV of the treated vessel. Patency will be assessed as patent versus occluded status only (patent defined as mPSV>0) and at the PARC cutoff (PSVR<2.4). [redacted]

5.5.3. Freedom from Major Adverse Events

Major adverse events (MAEs) are defined as: clinically-driven TLR; unplanned, unavoidable major amputation of the index limb; and death within 30 days of the index procedure. Kaplan Meier freedom from event rates and 95% confidence intervals will be summarized by treatment group [redacted]

5.5.4. Freedom from Target Lesion Revascularization

Angiographic images must be sent to the Angiographic Core Lab for adjudication of Target Lesion Revascularization (TLR) versus Target Vessel

Revascularization (TVR). If the angiographic core lab does not obtain images for assessment, the boundaries of the site reported retreatment location as compared to the baseline core lab reported lesion area will be assessed. Kaplan Meier freedom from event rates and 95% confidence intervals [redacted]

5.5.5. Freedom from Major Amputation

Freedom from unplanned, unavoidable major amputation of the index limb will be summarized [redacted] Kaplan Meier product-limit estimates and 95% confidence intervals will be provided by treatment group.

5.5.6. Change in Rutherford Category

Rutherford category will be summarized by treatment group [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5.5.11. Device Success

Device success is defined as the ability to achieve successful delivery and deployment of the DCB to the target lesion as described per IFU within 3 minutes of insertion without removal and use of an additional device. The percentage will be based on the number of DCB devices used.

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[redacted]

5.10 Adverse Events

Adverse events may be summarized by event type as well as seriousness and relatedness.