[redacted]

Assessment of the GORE® EXCLUDER® Conformable AAA Endoprosthesis in the Treatment of Abdominal Aortic Aneurysms

Statistical Analysis Plan

March 20, 2023

Study Acronym / Protocol #: AAA 13-03

[redacted]

Table of Contents

[redacted]

[redacted]

1.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical analyses planned to address the objectives of the AAA 13-03 clinical study. This SAP summarizes the analyses that will be performed to determine the safety and effectiveness of the Gore® EXCLUDER® Conformable AAA endoprosthesis (CEXC Device) when used for the treatment of abdominal aortic aneurysms (AAA). This SAP outlines tables, figures, and listings that are included in reports for the AAA 13-03 clinical study.

1.1 Study Success

In this two parallel substudy design, Gore will define study success on a substudy basis independent from each other.

1.1.1 Short Neck Substudy Success

The Short Neck Substudy is considered successful if both the safety and effectiveness performance goals are met.

1.1.2 High Neck Angulation Substudy Success

The High Neck Angulation Substudy is considered successful if both the safety and effectiveness performance goals are met.

2.0 Study Design Overview

This study is a prospective, multicenter, non-randomized clinical study with two parallel substudies designed to evaluate the safety and effectiveness of the CEXC Device for the treatment of AAA in patients with aortic proximal necks that are short in length and/ or highly angulated in nature. The substudies are described as follows:

Short Neck Substudy: Subjects with AAA having an aortic neck angulation ≤ 60° and an infrarenal aortic neck length ≥ 10 mm

High Neck Angulation Substudy: Subjects with AAA having an aortic neck angulation > 60° and ≤ 90° and an infrarenal aortic neck length ≥ 10 mm

2.1 Enrollment and AE Follow-up

Once the device delivery catheter has been introduced into the Subject's vasculature they are considered an enrolled Subject. Unsuccessful CEXC Device implant Subjects will be tracked for 30 days with all AEs reported. An unsuccessful CEXC Device Subject is defined as a person who underwent an open AAA repair or another stent graft at the time of initial procedure after successful introduction of the CEXC Device delivery catheter, and without CEXC Device system implantation. A patient who either was converted to open AAA repair prior to CEXC Device delivery catheter introduction or whose entire procedure was aborted prior to the CEXC Device delivery catheter introduction is not considered "unsuccessful" as they had not been enrolled in the study. Successful CEXC Device implant Subjects, defined as a Subject with the implantation of the CEXC Device system, will be followed according to the regimen described in **Section 5.2** of the protocol.

[redacted]

[redacted]

[redacted]

2.2 Objectives

2.2.1 Primary Objective(s)

The primary objective of the study is to assess the safety and effectiveness of the CEXC Device for the treatment of infrarenal AAA.

2.3 Design Summary

AAA 13-03 is a non-randomized, multi-center trial that will compare the composite safety and effectiveness endpoints to pre-specified performance goals. A total of 175 subjects will comprise the initial cohort of the study (95 within the High Neck Angulation Substudy and 80 within the Short Neck Substudy) [redacted] Subjects will be evaluated through hospital discharge and return for follow-up visits at one (1), six (6), 12, 24, 36, 48 and 60 months.

2.4 Study Endpoints

2.4.1 Primary Safety Endpoint (each substudy)

The primary safety endpoint will be a composite of the following within 30 days of the initial procedure based on the definitions provided by Chaikof et al[1]:

- Death
- Stroke
- Myocardial Infarction
- Bowel Ischemia
- Paraplegia
- Respiratory Failure
- Renal Failure
- Procedural Blood Loss > 1000 mL
- Thromboembolic events (limb occlusion and distal embolic events)

2.4.2 Primary Effectiveness Endpoint (each substudy)

Treatment success: Technical success (defined as successful access and deployment of all required CEXC Device components) and freedom from the following events:

- Type I endoleaks in the 12 month analysis window
- Type III endoleaks in the 12 month analysis window

[redacted]

- Migration ≥ 10 mm between the baseline and the 12 month analysis window
- AAA enlargement ≥ 5 mm with or without intervention between the baseline and the 12 month analysis window
- AAA rupture through the 12 month analysis window
- Conversion to open repair through the 12 month analysis window

The baseline assessment shall occur prior to the end of the one month study window for the Short Neck Substudy and within the first 90 post-operative days for the High Neck Angulation Substudy.

2.4.3 Secondary Endpoints (each substudy)

In addition to the primary effectiveness endpoints for each substudy population, a second group of effectiveness endpoints will be assessed for each substudy at each study follow-up interval (unless indicated otherwise). The endpoints will be reported descriptively and independent of the performance goals. The secondary effectiveness endpoints are defined as the following:

- Aneurysm-related mortality
- Stent fracture based on Core lab analysis (stent fracture will be described as a whole and classified into subclasses that describe their potential impact on CEXC Device proximal fixation.)
- Individual elements of the primary safety and effectiveness endpoints
- Reintervention
- Type II endoleak
- Type IV endoleak
- Index Procedure Blood Loss (initial procedure only)
- Index Procedure Time (initial procedure only)
- Length of Hospital Stay (initial procedure only)

2.5 Statistical Hypotheses

2.5.1 Primary Safety Endpoint (each substudy)

The analysis of the primary safety endpoint is intended to test the hypothesis that the safety of the CEXC Device exceeds the performance goal of 79% freedom from safety composite endpoint in each substudy separately.

The hypotheses are specified as follows:

$$H_0 : P_{SE} \leq 0.79$$
$$H_A : P_{SE} > 0.79$$

2.5.2 Primary Effectiveness Endpoint (each substudy)

The analysis of the primary effectiveness endpoint is intended to test the hypothesis that the effectiveness of the CEXC Device exceeds the performance goal of 80% freedom from effectiveness endpoint events in each substudy separately.

The hypotheses are specified as follows:

$$H_0 : P_{EE} \leq 0.80$$
$$H_A : P_{EE} > 0.80$$

2.6 Sample Size Assumptions

For the Short Neck Substudy primary safety endpoint, [redacted] a one sided test with alpha = 0.05, [redacted]

For the High Neck Angulation Substudy primary safety endpoint, [redacted] one sided test with alpha = 0.05, [redacted]

For the Short Neck Substudy primary effectiveness endpoint, [redacted] one sided test with alpha = 0.05, [redacted]

For the High Neck Angulation Substudy primary effectiveness endpoint, [redacted] one sided test with alpha = 0.05, [redacted]

2.7 Sample Size Calculations

[redacted]

80 Subjects will be utilized in the Short Neck substudy. [redacted]

The High Neck Angulation substudy [redacted]

sample size of 95 Subjects will be utilized. [redacted]

[redacted]

3.0 Study Treatment Arms

3.1 Test Arm

Patients with AAA are eligible for screening for participation in the study. The study has been designed with standard eligibility criteria to address any known or foreseeable factors that may compromise the outcome of the clinical investigation or the interpretation of results. Only patients who meet all of the Inclusion Criteria and none of the Exclusion Criteria should be enrolled. Gore will not provide any waivers or knowingly allow a patient to be enrolled in the study without meeting all of the described inclusion and exclusion criteria. Subjects will be considered enrolled once the device delivery catheter has been introduced into the Subject's vasculature.

3.2 Control Arm

There is no control arm in this study.

4.0 Study Data Collection

4.1 Study Data Collection Intervals

Subjects will be asked to return for follow-up visits at one (1), six (6), 12, 24, 36, 48, and 60 months post-treatment. At each follow-up visit, subjects will undergo an evaluation for adverse events. Evaluation methods will include a physical examination and spiral CTA of the abdomen and pelvis (non-contrast and contrast spiral CTA required at one (1) month visit) (**Table 1**).

Table 1. Subject Schedule of Events

Diagnostic Test	Pre-treatment	Treatment	1 month	6 months	Annually for 5 years
Physical examination	X		X	X	X
Creatinine concentration	X				
Spiral computed tomography (contrast)	X		X	X	X
Spiral computed tomography (non contrast)			X		
Angiography		X			

4.2 Follow-up Visit Windows

Follow-up visits will be scheduled at appointed times after the date of treatment. The Sponsor recognizes that Subjects may not be able to return for follow-up visits on the exact date required. Thus, a period during which each visit is allowed is demonstrated below (**Table 2**).

Table 2. Follow-up and Associated Visit Windows

Follow-up Visit	Ideal Window	Analysis Window (days)
Procedure	0	0
Discharge	Before hospital discharge	n/a

Post-Procedure	1 - 14	1 - 14
1 Month	23 - 44	15 - 89
6 Months	150 - 210	90 - 242
12 Months	275 - 455	243 - 546
24 Months	640 - 820	547 - 911
36 Months	1005 - 1185	912 - 1275
48 Months	1370 - 1550	1276 - 1640
60 Months	1735 - 1915	1641 - 2006

4.3 Data and Safety Monitoring Board

See **Section 9.6.1** of the protocol for information on the Data and Safety Monitoring Board.

4.4 Clinical Event Committee

See **Section 9.6.2** of the protocol for information on the Clinical Events Committee.

5.0 Statistical Analyses

5.1 Analysis Populations

The following populations will be used in various analyses of the data collected in the AAA 13-03 study:

1. All Enrolled Subjects - This population will consist of all enrolled Subjects

2. Safety Eligible Population (each substudy) - This population will consist of Initial Cohort Subjects with a follow-up visit at or after 30 days following initial CEXC Device implant procedure. Additionally, any Subjects with an eligible safety event, as defined in **Section 2.4.1**, even if they did not complete a follow-up visit at or after 30 days following initial procedure, will be included.

3. Primary Effectiveness Population

   Short Neck Substudy - This population will consist of Initial Cohort Subjects with both post-op (no later than one month study window) contrast-enhanced CT imaging and a 12 month follow-up visit that included contrast-enhanced CT imaging. Additionally, any Subjects with an eligible effectiveness event, as defined in **Section 2.4.2**, even if they did not complete the necessary follow-up visit or imaging to otherwise be included in the population, will be included.

   High Neck Angulation Substudy – This population will consist of Initial Cohort Subjects with both post-op (no later than 90 days) contrast-enhanced CT imaging and a 12 month follow-up visit that included contrast-enhanced CT imaging. If a subject without a 12 month contrast-enhanced CT imaging has post-12 month contrast-enhanced CT imaging at which there was no endpoint event identified by Core Lab (Type I Endoleak, Type III Endoleak, Migration, or Rupture) using the post 12-month contrast CT closest to the 12-month window, the subject will also be included in the analysis. Additionally, any Subjects with an eligible effectiveness

[redacted]

event, as defined in **Section 2.4.2**, even if they did not complete the necessary follow-up visit or imaging to otherwise be included in the population, will be included.

4. Secondary Effectiveness Populations (each substudy, each endpoint) - These populations will consist of Initial Cohort Subjects with an evaluable result for the specific variable.

5.2 Endpoint Variables

- Death – Site reported events.
- Stroke – CEC adjudicated site reported events through all follow-up time periods.
- Myocardial Infarction – CEC adjudicated site reported events through the 5-year follow-up periods.
- Bowel Ischemia – CEC adjudicated site reported events through the 5-year follow-up periods.
- Paraplegia – CEC adjudicated site reported events through the 5-year follow-up periods.
- Respiratory Failure – CEC adjudicated site reported events through the 5-year follow-up periods.
- Renal Failure – CEC adjudicated site reported events through the 5-year follow-up periods.
- Procedural Blood Loss > 1000 mL – Site reported events during initial procedure.
- Thromboembolic events – CEC adjudicated site reported events through the 5-year follow-up periods.
- Type I endoleaks – Core Lab reported events.
- Type III endoleaks –Core Lab reported events.
- Migration – Core Lab reported prosthesis or intercomponent migration.
- AAA enlargement – Using Core Lab reported data, the measurement closest to 30 days after initial implant will be subtracted from the measurement closest to 365 days after initial implant.
- AAA rupture –Core Lab reported events or CEC adjudicated site reported events through the 5-year follow-up periods.
- Conversion to open repair – CEC adjudicated site reported events through the 5-year follow-up periods.
- Aneurysm related mortality – CEC adjudicated site reported events through the 5-year follow-up periods.
- Stent fracture – Core Lab reported events.
- Reintervention – CEC adjudicated site reported events through the 5-year follow-up periods.
- Type II endoleak –Core Lab reported events.
- Type IV endoleak –Core Lab reported events.
- Index Procedure Time – Site reported during initial procedure.
- Length of Hospital Stay – Site reported during initial hospitalization.

5.3 Timing of Analyses

The primary effectiveness endpoint in the Short Neck Substudy will be analyzed after all Subjects eligible for the Short Neck Substudy Effectiveness Population have completed a follow-up visit in the 12 month window.

[redacted]

The primary effectiveness endpoint in the High Neck Angulation Substudy will be analyzed after all Subjects eligible for the High Neck Angulation Substudy Effectiveness Population have completed a follow-up visit in the 12 month window.

The primary safety endpoint will be analyzed in each substudy during the effectiveness analysis for that substudy.

5.4 Statistical Analysis of Endpoints

One-sided exact Clopper-Pearson confidence intervals for binomial proportions (alpha=0.05) will be constructed to test the primary safety and primary effectiveness hypotheses in each substudy. The null hypothesis will be rejected if the lower bounds of the 95% confidence interval estimating device effectiveness and safety exceeds the performance goal. This is equivalent to stating that the estimated effectiveness and safety must exceed the PG with a Type I error rate (alpha) of < 0.05.

All events must meet the protocol definition and will be adjudicated through the CEC process.

5.4.1 Primary Safety Endpoint Events

Primary safety endpoint events in each substudy will be computed as all enrolled Subjects experiencing an event meeting the definition in **Section 2.4.1**.

5.4.2 Primary Effectiveness Endpoint Events

Primary effectiveness endpoint events in each substudy will consist of all enrolled Subjects experiencing an event meeting the definition in **Section 2.4.2**.

5.5 Additional Analyses

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

5.5.5 Site Pooling

Site data will be pooled based on clinical comparability, *i.e.*, the study Sites followed a common protocol, the study was monitored to assure compliance with the protocol and applicable government regulations, and the data collection and handling procedures were the same at all study Sites. In order to justify pooling, 2 x k analyses of the primary safety endpoint and primary effectiveness endpoint results using generalized Fisher's exact tests will be performe [redacted]

[redacted]

[redacted]

6.0 Interim Analyses and Safety Monitoring Analyses (if applicable)

Safety data will be periodically reviewed by a Data Safety and Monitoring Board (DSMB), but these reviews will not constitute statistical analyses and therefore no adjustments for multiple testing will be necessitated. A comprehensive summary of all reported adverse events will be reviewed. Specific adverse events of clinical interest in this patient population will include, but are not limited to stroke, myocardial infarction, bowel ischemia, paraplegia, respiratory failure, thromboembolic events, and renal failure.

[redacted]

7.0 Analysis Specifications

[redacted]

7.3 Verification Level for Statistical Output

All necessary analysis datasets as well as tables referenced herein will be verified at Level I. All listings referenced herein will be verified at Level II. [redacted]

8.0 Data Sets, Tables, Figures, and Listings

At a minimum, the following set of Tables, Figures and Listings will be produced.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]