Post-Market Registry of the GORE® VIABAHN® VBX Balloon Expandable Endoprosthesis Implanted in Peripheral Vessels

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Statistical Analysis Plan

Study Acronym / Protocol #: VBX 17-04

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1.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical analyses planned to address the objectives of the VBX 17-04 registry is to collect post-market safety and performance data of the GORE® VIABAHN® VBX Balloon Expandable Endoprosthesis (VBX Stent Graft) in peripheral vessels in patients who require interventional treatment. This SAP summarizes the analyses that will be performed to determine the safety and effectiveness of the GORE® VIABAHN® VBX Balloon and outlines tables, figures, and listings that are included in reports for the VBX 17-04 clinical study.

2.0 Study Design Overview

Primary Objective(s)

The primary objective of the VBX 17-04 registry is to collect post-market safety and performance data of the GORE® VIABAHN® VBX Balloon Expandable Endoprosthesis (VBX Stent Graft) in peripheral vessels in patients who require interventional treatment

Design Summary

This registry utilizes a prospective, multicenter, non-randomized single-arm design to collect VBX Stent Graft clinical data in its use within the peripheral vasculature but outside of *de novo* iliac occlusive disease. Data will be representative of real-world, clinical use. Combined with data from long-term clinical investigations and reports from medical literature, real world clinical use data is integral for Gore to perform continuing assessments of its performance in addition to any long-term clinical investigations as well as reports in medical journals. To ensure that registry data is representative of real world use, the registry will employ broad inclusion / exclusion criteria to ensure its observational nature.

A maximum of 20 clinical registry sites (referred to as “sites” in the remainder of this document) in Europe will participate in this observational registry. Gore will maintain an updated list of all principal investigators, site names, and addresses. This list shall be kept separately from this protocol. From all enrolled subjects the first 280 implanted patients will be evaluated for the registry.” No one site can contribute more than 35% of the total patient population (98 patients). There are no pathology-specific limitations at the registry or site level. The anticipated accrual rate is approximately 10 implanted patients per month for a total accrual period of approximately 28 months based upon the rapidity of site-start-up.Study Endpoints

Study Endpoints

2.1.1 Primary Endpoint(s)

The primary endpoint of the VBX 17-04 registry is a composite of the following events reported within 30 days of treatment.

- Procedural Success
- Freedom from VBX Stent Graft-related SAE

The first component, Procedural Success, describes the technical function of the VBX Stent Graft at the time of implant. The other component event, freedom from VBX Stent Graft-related Serious Adverse Event (SAE), is a description of short-term, device safety. Possible endpoint events will be identified from site reports and adjudicated by a Clinical Events Committee (CEC) for reporting eligibility.

2.1.2 Secondary Endpoint(s)

Selected events that are illustrative of the device's potential impact to a patient from a safety perspective, overall device function described as patency or device durability captured as device integrity are to be as the registry's secondary endpoints. Possible endpoint events will be identified from site reports with some secondary endpoints within scope of CEC adjudication.

The secondary endpoints for the VBX 17-04 registry are the following:

- VBX Stent Graft-related death within 30 days post-treatment
- Procedural-related death within 30 days post-treatment
- Procedural-related SAE within 30 days post-treatment
- VBX Stent Graft patency (primary, primary assisted, secondary) through 30 days post-treatment
- VBX Stent Graft patency (primary, primary assisted, secondary) through five years post-treatment
- VBX Stent Graft-related SAE through five years post-treatment
- VBX Stent Graft-related death through five years post-treatment
- Loss of device integrity through five years post-treatment
- Limb salvage through five years post-treatment

Table 1. Protocol Definitions

Protocol Term	Definition
Procedural Success	Technical Success (successful access, delivery, accurate deployment, and withdrawal of catheters) with patent VBX Stent Graft at end of procedure
Patency	**Primary** - Uninterrupted patency with no procedures performed on or at the margins of the treated segment. **Primary Assisted** - Any procedure performed in the treated segment before thrombosis that might prevent eventual failure. **Secondary** - Any procedure that restores patency after thrombosis.
Loss of Device Integrity	Defined as any of the following: • Device damage that compromises device functionality (stent fractures, graft tears, cuts, holes, delamination) • Transient (compression) or permanent stent-graft collapse (invagination) following complete device deployment, resulting in an overall reduction in the vessel luminal diameter
Limb Salvage	Freedom from Major Tissue Loss—extending above transmetatarsal level; functional foot no longer salvageable[28]
Reintervention	An additional unanticipated interventional or surgical procedure (including conversion to open surgery), related to the device (including withdrawal of the delivery system) or procedure. Anticipated or unanticipated status will be determined at the discretion of the investigator.

	• This includes reintervention to the VBX device used during the Index procedure and not in non-VBX treatment areas
Type I endoleak	A sealing failure at one of the attachment sites of the graft to the vessel wall providing arterial flow alongside the graft and into the perigraft space. • Type Ia- Proximal attachment site • Type Ib- Distal attachment site • Type Ic- Inadequate seal at distal landing zone of branch vessel device
Type II endoleak	Retrograde flow through collateral vessels into the aneurysmal sac.
Type III endoleak	• Type IIIa- Arterial flow from module disconnection • Type IIIb- Arterial flow from fabric disruption
Type IV endoleak	Arterial flow through porous fabric

Statistical Hypotheses

No formal hypothesis will be tested in the study

Sample Size Assumptions

The assumptions that provided basis for the required sample size included Clinical success of 97.1% and freedom from device or procedure related SAEs to be 93.6%

Sample Size Calculations

Two hundred eighty (280) patients will be implanted with the VBX Stent Graft across multiple pathologies. The sample size of 280 patients was considered adequate to estimate study outcomes with reasonable precision and to have sufficient subjects enrolled within each indication. The sample size was determined by Gore to characterize broad device use across device indications. In combination with strategic selection of participating registry sites, this number should be sufficient to describe the study endpoints with less than 6% margin of error.

3.0 Study Treatment Arms

Test Arm

Not applicable for registry

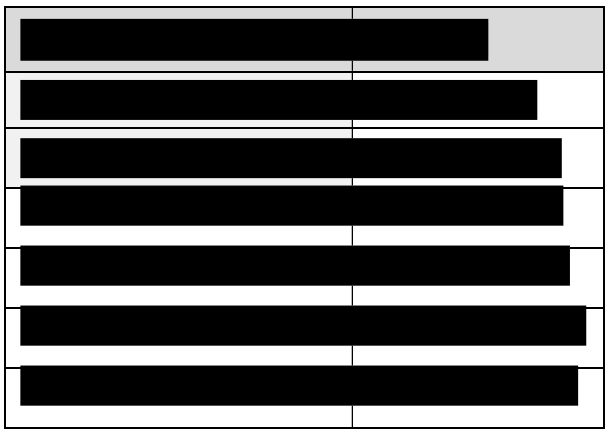
Control Arm(s)

Not applicable for registry

4.0 Study Data Collection

To aid in registry reporting, [redacted]

[redacted]



The Clinical Data Management System (CDMS) will be used to capture and maintain study data as per Clinical Data Management Plan describing the procedures for verification, validation, and security of the CDMS. The Clinical Data Management Plan will describe and document procedures regarding data management processes for this investigation.

a) Data Collection Methods

The CDMS will be the database of record for the protocol and subject to regulatory inspections and quality assurance review. All users will be trained to use the CDMS and will comply with study specific guidelines / instructions as well as applicable regulatory requirements.

Subject data will be collected using protocol-specific case report forms (CRF). Site staff will enter data directly into the CRF for transmission to the sponsor. The sites will be notified of any significant amendments to the CRFs.

b) Data Clarification and Correction

Once entered, data will be evaluated to confirm that it is complete, consistent, and logically sound. If changes to the data in the CDMS are required, all changes, reasons for changes, and persons making the changes will be captured in the CDMS's audit trail. Gore will perform periodic data reviews throughout the entire study. Procedures and documentation for regular and ongoing data review are described in the Clinical Data Management Plan.

c) CRF Completion Schedule

Entry of patient data into the EDC system cannot occur prior to the collection of the patient's informed consent to participate in the registry. All registry data is targeted to be entered into the appropriate CRF within two weeks of collection, however, data outside this window will not be considered a protocol deviation.

5.0 Clinical Event Committee

An independent Clinical Event Committee (CEC) will review safety- related, clinical events during the study to ensure the consistency of endpoints reported by the site. The VBX 17-04 CEC will be comprised of an interdisciplinary team of three members with pertinent expertise who are not directly involved in the conduct of the study.

The scope of the CEC activity includes the following:

1. General review and adjudication of Serious Adverse Events (SAEs) to include:
   a. Adjudication on the SAE designation
   b. Adjudication of the relationship of the SAE to the study device, procedure, or unrelated
2. Protocol Deviation review (as appropriate)
   a. Due to the potential safety concern, protocol deviations associated with inclusion/exclusion criteria will be reviewed and the CEC will assess their risk for significant medical events that would not be expected from a subject that met all inclusion/exclusion criteria.

6.0 Statistical Analyses

No formal hypothesis will be tested for this registry. The registry is designed for broad data collection across multiple pathologies to aid in Gore's continuing assessment of risk with the real world use of the VBX Stent Graft. Due to the commercial nature of the device, the registry will not employ a pass / fail determination against pre-defined hypotheses but will instead measure observed performance of the entire registry population using a two-sided, exact binomial 95% confidence intervals for the primary outcomes.

i) Timing of Analyses

The final analysis will be performed when all subjects have completed their 5 years follow-up visit or have been withdrawn from the registry. Analyses will be performed as needed for annual reports. Analyses at any other time may be performed at the discretion of Gore.

ii) Analysis Populations

All enrolled patients meeting the inclusion / exclusion criteria and treated with the VBX Stent Graft will be included in the primary and secondary endpoint analyses.

iii) Pooling of Data

The VBX Stent Graft may be used in treatments that may differ by type of treatment (elective vs. emergent), patient risk (high vs. low / moderate) or role in treatment (primary repair vs. combinatorial repair). In each of these indications, the mechanism of introduction and device delivery will remain the same along with intended device function (lesion exclusion / vessel patency). The use of balloon-expandable stents are a well-known and practiced endovascular therapy that is not expected to differ between selected registry sites. As such, there is no concern in regards to pooling data from different European countries or sites together for analysis.

Gore may perform analyses to detect differences in device experience according to gender, age or pathology treated.

iv) Statistical Analysis of Primary Endpoint(s)

The two primary endpoints - procedural success and freedom from device-related SAE at 30 days will be presented descriptively as percentages with 95% confidence intervals. Subjects with missing information on the primary outcomes will not be included in the analysis.

v) Statistical Analysis of Secondary Endpoint(s)

Analysis of the secondary endpoints—device related death at 30 days, procedural related death at 30 days, procedural related SAE at 30 days, device patency at 30 days, in addition, device patency, device-related SAEs, device related deaths and loss of device integrity will be reported yearly as both yearly percentages and rates. Data will be presented descriptively with 95% confidence intervals, where appropriate. Subjects with missing information on these outcomes will not be included in the analysis.

vi) Analysis by Treatment Category

Individual device treatment indications will be categorized into larger groups “Treatment Categories” based upon either similar device function or purpose. Combining treatment indications into larger groups will permit the analysis of general treatment concepts where an analysis based upon an individual indication would not be feasible. Analyses of a Treatment Category will be performed descriptively with no pre-determined hypothesis.

vii) Analysis of Individual Treatment Indications

At the conclusion of enrollment, an evaluation of the distribution of device use across individual pathologies will be performed. If feasible, device experience by indication will be tabulated for descriptive analysis.

7.0 Interim Analyses and Safety Monitoring Analyses (if applicable)

[redacted]

8.0 Analysis Specifications

[redacted]

Statistical Output Specifications

[redacted]

Verification Level for Statistical Output

- All Analysis Datasets – Level I

- All Tables – Level I
- All Listings – Level II

9.0 Data Sets, Tables, Figures, and Listings

[redacted]

- [redacted]

10.0 References

[redacted]