Evaluation of the GORE® EXCLUDER® Thoracoabdominal Branch Endoprosthesis in the Treatment of Thoracoabdominal and Pararenal Aortic Aneurysms

Protocol Number: AAA 17-01

[redacted]

24-Mar-2023

W. L. Gore & Associates, Inc.
Medical Products Division

PROTOCOL SUMMARY

Study Title	Evaluation of the GORE® EXCLUDER® Thoracoabdominal Branch Endoprosthesis in the Treatment of Thoracoabdominal and Pararenal Aortic Aneurysms
Protocol Number	AAA 17-01
[redacted]	
IDE Number	G150071
Sponsor	W. L. Gore & Associates, Inc. [redacted] Telephone: 800-437-8181
Study Design	Prospective, non-randomized, multicenter study with two independent arms: • Primary Study Arm – TAAA requiring only TAMBE System. Hypothesis-driven analysis. • Secondary Study Arm – TAAA requiring TAMBE System and CTAG Device(s). Non-hypothesis-driven analysis.
Study Objective	Assess the safety and effectiveness of the TAMBE Device in the treatment of thoracoabdominal and pararenal aortic aneurysms
Co-Primary Study Endpoints	1. Uncomplicated Technical Success / Procedural Safety Co-Primary Endpoint A composite of the following events: • Device Technical Success at the time of the index endovascular procedure • Procedural Safety events within 30 days of index procedure: 2. Clinically Significant Reintervention / Lesion-Related Mortality Co-Primary Endpoint (12 months post-treatment) • Clinically Significant Reintervention (*using protocol definition*) • Lesion-Related Mortality
Subject Population	Subjects with thoracoabdominal or pararenal aortic aneurysms requiring treatment Primary Study Arm: Adapted Crawford Type IV TAAA and Pararenal aneurysms (n= 102)

	Secondary Study Arm: Adapted Crawford Type I-III (n= 20 - 100) Continued Access (Primary Study Arm): Adapted Crawford Type IV TAAA and Pararenal Aneurysms (n=up to 65)
Number of Implanted Subjects	Minimum: 122 implanted subjects, Maximum: 202 implanted subjects with up to 65 additional subjects implanted in Continued Access (Primary Study arm).
Number of Sites	Up to 45 sites in the United States and Europe
Coordination PI	[redacted]
Brief Inclusion Criteria	• Aortic aneurysm involving the visceral vessels requiring treatment defined as at least one of the following: o Fusiform aneurysm diameter ≥ 5 cm o Saccular aneurysm (no diameter requirement) o Rapid aneurysm growth (≥ 5 mm in one year) • An Informed Consent Form signed by Subject or legal representative • Appropriate aortic anatomy to receive the TAMBE Device defined as all of the following: o For the TAMBE Aortic Component, proximal aortic landing zone diameters between 22 -34 mm o Proximal seal zone ≥ 20 mm in length
Brief Exclusion Criteria	• Prior open, aortic surgery of the ascending aorta or aortic arch • Myocardial infarction or stroke within 1 year of treatment (staged or index procedure) • Previous instance of Heparin Induced Thrombocytopenia type 2 (HIT-2) or known hypersensitivity to heparin • Renal insufficiency (creatinine value > 1.8 mg/dL, GFR < 30, or patient undergoing dialysis)
Expected Time to Complete Enrollment	Primary Study Arm Subject Accrual: 27-32 months Follow-up – 5 years from last subject enrollment
Brief Schedule of Events	Screening Pre-Treatment Treatment Discharge Follow-up (30 day, 3, 6, 12 months and annually thru 5 years)

STUDY and VENDOR INFORMATION

Study Information	
Study Contact Information	General e-mail: [redacted] Study manager information Emergency Contact *Located in the study Regulatory Binder*
Study Financing	Financed by W. L. Gore & Associates, Inc.
Data Monitoring Committees *(Gore-coordinated)*	Clinical Events Committee (CEC) Data Safety Monitoring Board (DSMB)
Emergency and Compassionate Use	Supported, with conditions
Reimbursement Information	Reference the Claims Binder
Study Roster	List of sites (addresses, principal investigator, emergency contact information) *Located in the study Regulatory Binder*
Vendor Information	
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Evaluation of the GORE® EXCLUDER® Thoracoabdominal Branch Endoprosthesis in the Treatment of Thoracoabdominal and Pararenal Aortic Aneurysms

Statistical Analysis Plan

Study Acronym / Protocol #: AAA 17-01

Table of Contents

1. Introduction

This Statistical Analysis Plan (SAP) describes the statistical analyses planned to address the objectives of the AAA 17-01 clinical study. This SAP summarizes the analyses that will be performed to determine the safety and effectiveness of the Thoracoabdominal Branch Endoprosthesis (TAMBE) Device when used for endovascular repair of thoracoabdominal and pararenal aortic aneurysms in subjects with appropriate anatomy. This SAP outlines tables, figures, and listings that are included in reports for the AAA 17-01 clinical study.

1.1 Study Success

Study success will be defined as rejecting the null hypotheses from both the Uncomplicated Technical Success Endpoint and the Clinically Significant Reintervention end points.

2. Study Design Overview

This will be a prospective, non-randomized, two-armed, multicenter study conducted at up to forty-five (45) Clinical Investigative Sites (referred to as "sites" in the remainder of this document) in the United States and Europe. A minimum of 122 subjects, up to a potential maximum of 202 subjects, will be implanted with the TAMBE Device across two independent study arms as described below.

- Primary Study Arm – Hypothesis-driven analysis, Thoracoabdominal aneurysms (TAAAs) which are anatomically suitable for treatment with the TAMBE Device and do not require proximal extension with a CTAG Device (N=102). This arm will be limited to pararenal aortic aneurysm and adapted Crawford Type IV TAAAs.
- Secondary Study Arm – Non hypothesis-driven analysis, TAAAs which are anatomically suitable for treatment with the TAMBE Device and would require proximal extension with CTAG Device(s). This arm will include adapted Crawford Type I-III TAAAs. (N=20-100 Subjects)

Up to 65 additional subjects may be implanted in the Continued Access Phase under the Primary Study Arm only. All sites will be allowed to enroll in the Continued Access Phase, and all sites and subjects will be treated and followed in the same manner as the Core Clinical Investigation.

- The reduced profile VBX Device cohort (a subset of the Continued Access phase) will follow the TAMBE protocol: all primary, secondary, and other endpoints will be collected for these subjects as per protocol in the same manner as for the other cohorts. The Target Vessel Technical Success of the reduced profile VBX Device for each vessel will also be assessed.

- To assess the compatibility of reduced profile VBX Device as a side branch component in conjunction with the TAMBE Aortic Component (AC), the following endpoints will be summarized at a subject level:

- Uncomplicated Technical Success at Index Procedure
- Procedural Safety data through 30-day follow-up
- Summary of AEs through 30-day follow-up including Type Ic and IIIc Endoleaks

2.1 Objectives

2.1.1 Primary Objective(s)

The primary objective of the study is to determine whether the GORE® EXCLUDER® Thoracoabdominal Branch Endoprosthesis is safe and effective in the treatment of thoracoabdominal and pararenal aortic aneurysms.

The study will utilize separate, independent hypothesis-driven analyses in order to make this determination in the study's target population of pararenal aortic aneurysm subjects and adapted Crawford Type IV thoracoabdominal aneurysm subjects.

Gore recognizes that the TAMBE Device, in combination with proximal CTAG Device extension, may have applicability to Crawford Type I-III thoracoabdominal aneurysm subjects. Hypothesis-driven assessments will not be performed in this secondary study arm population with device performance characterized for potential future applications.

2.1.2 Secondary Objective(s)

There are no Secondary Objectives specified for this study.

2.2 Design Summary

AAA 17-01 is a prospective, non-randomized, multi-center trial that will compare the Uncomplicated Technical Success / Procedural Safety and Clinically Significant Reintervention / Lesion Related Mortality co-primary endpoints to pre-specified performance goals. A minimum of 122 subjects and a maximum of 202 subjects will be enrolled and implanted across both sub-groups; 102 Subjects within the Primary Study Arm and between 20 and 100 Subjects within the Secondary Study Arm, with a minimum requirement of 20 combined adapted Crawford Type I and Type II aneurysms. Subjects will be evaluated through hospital discharge and return for follow-up visits at one (1), three (3), six (6), 12, 24, 36, 48 and 60 months. This is a confirmatory study.

2.3 Study Endpoints

2.3.1 Primary Endpoint(s)

There are two Co-Primary Endpoints used in this study: Uncomplicated Technical Success / Procedural Safety and Clinically Significant Reintervention / Lesion Related Mortality. A hypothesis test will be conducted on each Co-Primary Endpoint.

1. Uncomplicated Technical Success / Procedural Safety Co-Primary Endpoint (evaluated through 30 days post procedure)

Table 1 displays the components for the Uncomplicated Technical Success Primary Endpoint, along with their definitions, time each item is evaluated and the final source data for each item. Definitions provided are referenced from the Clinical Protocol, Section 3.3.

Table 1: Summary of Uncomplicated Technical Success Primary Endpoint

Outcome	Definition (per Clinical Protocol Section 3.3)	Endpoint Time Evaluated	Final Source Data
Uncomplicated Technical Success			
Successful access and delivery	All Gore devices are successfully tracked from the access site to the intended implantation site and released from the deliver catheter successfully without the need for unanticipated corrective intervention related to delivery.	TAMBE Device Index procedure	Site data
Successful and accurate deployment	Deployment of all required endovascular device components in the planned location: · Patency of required aortic endovascular grafts with absence of device deformations (e.g., kinks) requiring unplanned placement of a non-TAMBE device component* within the endovascular graft; · Patency of all branch devices with absence of device deformations (e.g., kinks) requiring unplanned placement of any non-TAMBE device component* within the branches**; * TAMBE components include the aortic component, distal bifurcated component, iliac extenders, contralateral legs, VBX component and CTAG Device. **Implantation of bare metal stents to smooth the transition from the VBX to the uncovered branch vessel will not count against technical success if the procedure otherwise meets the definition of technical success. Use of non-TAMBE devices to correct iatrogenic complications in the treated aorta or branch vessels would be considered technical failures.	TAMBE Device Index procedure	Site Reported and CEC Adjudication[1]
Successful withdrawal	Successful withdrawal of the delivery systems, without a need for corrective intervention related to withdrawal	TAMBE Device Index procedure	Site data
Procedural Safety			

Outcome	Definition (per Clinical Protocol Section 3.3)	Endpoint Time Evaluated	Final Source Data
Aortic Rupture	Rupture in the stented segment of the aorta verified with direct observation or CT scan	30 days	CEC adjudication
Lesion-related mortality	Defined as all deaths during hospitalization for index endovascular procedure and within 30 days of the index endovascular procedure or any secondary procedures due to the treated pathology, or the effectiveness of the endovascular repair (e.g., procedures to treat retrograde dissections, losses of patency, losses of device integrity, endoleaks, migrations, aortic expansions, aortic ruptures) and any deaths related to the treated pathology or endovascular graft (e.g., aneurysm rupture, retrograde dissection leading to fatal cardiac tamponade), unless evidence is available to demonstrate that the death is not lesion related	30 days or in-hospital for index endovascular procedures	
Permanent paraplegia	Paraplegia secondary to spinal cord ischemia identified within 30 days of the index endovascular procedure combined with spinal cord ischemia scale grade of "3" at the one-month follow-up visit. The grading system for spinal cord ischemia is described in TEVAR reporting standards	Event reported within 30 days of endovascular procedure without resolution at one month follow-up	
Permanent paraparesis	Paraparesis secondary to spinal cord ischemia identified within 30 days of the index endovascular procedure combined with spinal cord ischemia scale grade of "2" at the one-month follow-up visit. The grading system for spinal cord ischemia is described in TEVAR reporting standards	Event reported within 30 days of endovascular procedure without resolution at one month follow-up	
New onset renal failure requiring dialysis	New onset sustained renal failure identified within 30 days of the index endovascular procedure, combined with need/requirement for dialysis at the one month follow- up visit	Event reported within 30 days of endovascular procedure without resolution at one month follow-up	
Severe bowel ischemia	Bowel ischemia resulting in bowel resection or fatal outcome	30 days	
Disabling stroke	Stroke was assessed using the Modified Rankin Scale. Stroke identified as having occurred within 30 days of the index endovascular procedure, combined with mRS ≥2 with an increase from baseline of at least one grade at 90 days Modified Rankin Score was completed by an allied health staff member who successfully completed mRS certification or licensed medical professional	120 days (30 days for Stroke Events, plus 90 days for mRS measurements)	

[1]As part of successful and accurate deployment, the CEC will adjudicate use of non-TAMBE devices to correct iatrogenic complications in the treated aorta or branch vessels.

2. Clinically Significant Reintervention / Lesion Related Mortality Co-Primary Endpoint (12 months post-treatment)

Table 2 contains the definition, endpoint time evaluated, and the final source data for the components of the Clinically Significant Reintervention / Lesion Related Mortality Co-Primary Endpoint. This endpoint is evaluated at 12 months post-treatment.

Table 2: Summary of Clinically Significant Reintervention / Lesion Related Mortality Co-Primary Endpoint

Outcome	Definition (per Clinical Protocol Section 3.3)	Endpoint Time Evaluated	Final Source Data
Clinically Significant Reintervention			
Clinically-Indicated Condition	An untreated device seal zone endoleak, target-lesion growth (> 5 mm in maximum diameter) or post-treatment TAAA rupture without reintervention at the 12 Month window follow-up visit	12 mo f/u visit	Core Lab (aneurysm size and endoleak) CEC Adjudication (TAAA rupture) Site Data (reintervention)
Device Effectiveness	A compromise of a device seal zone or loss of device integrity (e.g., device kink or collapse) requiring placement of an additional stent or stent-graft	12 mo f/u visit	CEC adjudication
Subject Safety	Total occlusion of a device component, use of a bypass graft or the performance of an open conversion in order to maintain bodily vessel function	12 mo f/u visit	
Complicated Device System Prophylaxis	Any device-related intervention requiring hospitalization, or extension of hospitalization, of three days or more	12 mo f/u visit	
Lesion-related mortality			
Lesion-related mortality	All deaths during hospitalization for index endovascular procedure and within 30 days of the index endovascular procedure or any secondary procedures due to the treated pathology, or the effectiveness of the endovascular repair (e.g., procedures to treat retrograde dissections, losses of patency, losses of device integrity, endoleaks, migrations, aortic expansions, aortic ruptures) and any deaths related to the treated pathology or endovascular graft (e.g., aneurysm rupture, retrograde dissection leading to fatal cardiac tamponade), unless evidence is available to demonstrate that the death is not lesion related	12 mo f/u visit	CEC adjudication

2.3.2 Secondary Endpoint(s)

Table 3 contains the definitions, endpoint time evaluated and source data for the secondary endpoints. The majority of definitions in **Table 3** are sourced from the Clinical Protocol Section 3.3. Secondary Endpoint items marked with an asterisk (*) are defined by this document.

Table 3: Secondary Endpoint Definitions

Outcome	Definition	Endpoint Time Evaluated	Final Source Data
Standard Procedure / Hospitalization Metrics			
Aneurysm-related mortality	Defined as all deaths during hospitalization for index endovascular procedure and within 30 days of the index endovascular procedure or any secondary procedures due to the treated pathology, or the effectiveness of the endovascular repair (e.g., procedures to treat retrograde dissections, losses of patency, losses of device integrity, endoleaks, migrations,	30 Days	CEC

Outcome	Definition	Endpoint Time Evaluated	Final Source Data
	aortic expansions, aortic ruptures) and any deaths related to the treated pathology or endovascular graft (e.g., aneurysm rupture, retrograde dissection leading to fatal cardiac tamponade), unless evidence is available to demonstrate that the death is not lesion related.		
Individual elements of Procedural Safety • Aortic Rupture • Lesion-related mortality • Permanent paraplegia • Permanent paraparesis • New onset renal failure requiring dialysis • Severe bowel ischemia • Disabling stroke	Reference **Table 1** for definitions for these elements	Reference **Table 1**	Reference **Table 1**
Procedural blood loss	Estimated Blood Loss during Index Procedure (mm)*	Index Procedure	Site
Access-related complications	An Adverse Event determined by Site to be related to vascular access*	30 Days	Site
Procedural time	Duration of Index Procedure (minutes) [the time of incision will indicate the start time and the finish time is the time of closure]. *	Index Procedure	Site
Stage Procedure Time	Duration of Stage Procedure (minutes) [the time of incision will indicate the start time and the finish time is the time of closure]. *	Stage Procedure	Site
Length of hospital stay	Number of Days Subject stayed in hospital (from admission date to discharge date). *	Initial Hospitalization of Index Procedure	Site
Stage procedure length of hospital stay	Number of Days Subject stayed in hospital for stage procedure (from admission date to discharge date). *	Stage Procedure	Site
Extended Technical Clinical Success	Subjects who present within the 30-Day follow-up with no Type I or Type III endoleak, as evaluated by CTA, and free from device-related intervention	30 Days	Core Lab
Aortic Stent-Graft Effectiveness Measures			
Type I endoleak	Endoleak arising from the proximal or distal sealing zone of a device perfusing the aneurysm	Through 12 Months	Core Lab
Type IA endoleak	Inadequate seal at the proximal end of the device placed in the aorta	Through 12 Months	Core Lab
Type IB endoleak	Inadequate seal at the distal end of the device placed in iliac vessel	Through 12 Months	Core Lab
Type IC endoleak	Inadequate seal at the distal end of a device placed inside branch vessel	Through 12 Months	Core Lab

Outcome	Definition	Endpoint Time Evaluated	Final Source Data
Type II endoleak	Endoleak arising from a patent branch vessel perfusing the aneurysm, e.g., lumbar or inferior mesenteric branch	Through 12 Months	Core Lab
Type III endoleak	Endoleak arising from the component junction(s) of the prosthesis or due to damage to the graft material perfusing the aneurysm.	Through 12 Months	Core Lab
Type IIIA endoleak	Modular disconnection or apposition failure	Through 12 Months	Core Lab
Type IIIB endoleak	Graft tear	Through 12 Months	Core Lab
Type III General endoleak	A Type III endoleak whose source cannot be differentiated between an intercomponent junction or graft tear	Through 12 Months	Core Lab
Type IV endoleak	Endoleak of whole blood through the graft fabric perfusing the aneurysm	Through 12 Months	Core Lab
Indeterminate endoleak	Endoleak perfusing the aneurysm without a definitive source	Through 12 Months	Core Lab
Device Migration	Longitudinal movement of all or part of the device for a distance ≥10 mm, as confirmed by CT scan, relative to anatomical landmarks and device positioning at the first post-operative CT scan	Through 12 Months	Core Lab
TAAA enlargement	An increase in the maximum aneurysm diameter of 5 mm or more relative to the first post-operative CT scan within the 30 day follow-up window	Through 12 Months	Core Lab
Severe distal thromboembolic events	Ischemic events related to the device from tissues distal to the device implantation site sufficiently debilitating to necessitate bypass, open surgical intervention, limb amputation or leading to death	Through 12 Months	CEC
Aortic Rupture	Rupture in the stented segment of the aorta verified with direct observation or CT Scan*	Through 12 Months	CEC
Device or procedure-related laparotomy	An adverse event assessed by the site as being device or procedure-related that led to a laparotomy *	Through 12 Months	Site
Conversion to open repair	A reintervention that resulted in explant of the device and open surgical repair*	Through 12 Months	Site
Aortoiliac device limb occlusion	An occlusion in the distal bifurcated component, contra-lateral limb component, contra-iliac extender component, or the ipsi-lateral extender component*	Through 12 Months	Core Lab
Loss of device integrity	Defined as any of the following: • Wire fracture identified in the sealing row stents of either the aortic, branch or iliac components • Transient (compression) or permanent stent-graft collapse (invagination) following complete	Through 12 Months	Core Lab

Outcome	Definition	Endpoint Time Evaluated	Final Source Data
	device deployment, resulting in an overall reduction in the aortic, branch or iliac vessel luminal diameter		
Primary patency Adapted Study Definition	Blood flow without occlusion maintained through the device after implant without an intervention.	Through 12 Months	Site and Core Lab
Assisted primary patency Adapted Study Definition	Blood flow maintained through the device after implant regardless of re-interventions performed (without occlusion)	Through 12 Months	Site and Core Lab
Secondary patency Adapted Study Definition	Blood flow through the device regardless of reinterventions performed (with or without occlusion) and freedom from surgical bypass	Through 12 Months	Site and Core Lab
All reinterventions	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. These will not include unanticipated, corrective intervention at the access site(s), or device intervention to address non-treatment area issues	Through 12 Months	Site
Branch Vessel Device Effectiveness Measures			
Branch vessel patency	Primary, Assisted Primary, Secondary Patency	12 Months	Site and Core Lab
Acute kidney injury	>50% decrease in eGFR within 30 days of TAMBE Device treatment when compared to pre-treatment serum creatinine value	30 days	Site
Renal function deterioration	A sustained >25% decrease in eGFR over two consecutive study visits following TAMBE Device treatment when compared to pre-treatment serum creatinine value	12 Months	Site

2.4 Statistical Hypotheses

The analysis of the Uncomplicated Technical Success / Procedural Safety endpoint is intended to test the hypothesis that the safety of the TAMBE Device exceeds the performance goal of 80% technical success. This analysis will be performed on the Primary Study Arm (pararenal aortic aneurysms and adapted Crawford Type IV TAAA). The analysis of the Clinically Significant Reintervention / Lesion Related Mortality endpoint is intended to test the hypothesis that the effectiveness of the TAMBE Device exceeds the performance goal of 68% free from clinically significant reintervention / lesion related mortality events.

The hypotheses are specified as follows:

<u>Uncomplicated Technical Success / Procedural Safety Hypothesis:</u>

$H_0 : P_{UCT} \leq 0.80$

$H_A : P_{UCT} > 0.80$

Where P_{UCT} denotes the proportion of subjects that achieve technical success.

Clinically Significant Reintervention / Lesion Related Mortality Hypothesis:

$H_0 : P_{CSR} \leq 0.68$

$H_A : P_{CSR} > 0.68$

Where P_{CSR} denotes the proportion of subjects that achieve freedom from clinically significant reintervention.

2.5 [redacted]

[redacted]

2.6 Sample Size Calculations

Sample size calculations were determined using PASS 13.0.8 ("Tests for One Proportion using Proportions" and "Exact" options).

The sample size calculation was motivated primarily by the Clinically Significant Reintervention Hypothesis / Lesion Related Mortality, since that would require more subjects to properly power than the Uncomplicated Technical Success / Procedural Safety hypothesis.

At least 86 are required to maintain > 80% power for the Clinically Significant Reintervention / Lesion Related Mortality Hypothesis. Assuming a 15% loss-to-follow-up rate, 102 subjects are sufficient for achieving the objective (with 81.48% power). For uncomplicated technical success, a sample size of 102 enrolled and implanted subjects (86 expected evaluable subjects) will yield a power of 93.41%. We expect the results of these hypotheses tests to be correlated, so an overall power calculation of the product of the two powers is inappropriate.

Expected accrual of subjects for the Primary Study Arm is 27 to 32 months.

3. Study Treatment Arms

3.1 Test Arms

There will be a Primary Study Arm and a Secondary Study Arm in this study.

- Primary Study Arm – Hypothesis-driven analysis, TAAAs which are anatomically suitable for treatment with the TAMBE System and do not require proximal extension with a CTAG Device (N=102)

- Secondary Study Arm – Non hypothesis-driven analysis, TAAAs which are anatomically suitable for treatment with the TAMBE System and would require proximal extension with CTAG Device(s) (N=20 minimum,100 maximum as aggregate total of all types). Subjects that undergo placement of the CTAG Device but do not complete the implant of the TAMBE Device whether by subject choice or Investigator discretion will only have their adverse events reported through 30 days after implant and withdrawn from the study.

3.2 Control Arm(s)

There are no control arms in this study.

4. Study Data Collection

Subjects will be evaluated, at a minimum, using the schedule of events described in **Table 4**. The timing of study evaluations will be done according to the schedule defined in **Table 5**. Investigators will be held responsible for the performance of all Protocol-required testing at their respective time points, including testing done at institutions different than the implanting study site. It is highly recommended that subjects return back to their centers of enrollment for follow-up evaluations to foster testing compliance and continuity of care.

Sites are to schedule all study testing to be performed within the ideal visit window; however, any available data collected in the analysis window will be summarized as occurring within the given window. Data collected outside the ideal window, but within the analysis window will not be considered a protocol deviation.

4.1 Study Collection Intervals

Subjects will be asked to return for follow-up visits at one (1), three (3), six (6), 12, 24, 36, 48, and 60 months post-treatment. At each follow-up visit, subjects will undergo an evaluation for adverse events.

Table 4: Schedule of Events

	Pre-treatment (Screening)	Treatment	Hospital Discharge	One Month	Three Months	Six Months	Annually through 5 Years
Informed Consent	X						
Demographics and Medical History	X						
Risk Scales (ASA, NYHA, SVS)	X						
Physical examination	X		X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X
Medication Review	X		X	X	X	X	X
Modified Rankin Scale [a,b]	X		X	X	X *If applicable*	X	
Spinal Cord Ischemia Scale [a]	X		X	X		X	

NIH Stroke Scale[c]	X		X *If applicable*				
SF-36 Questionnaire	X			X	X	X	X
Serum Creatinine Concentration	X		X	X	X	X	X
Spiral CTA (contrast)[d,]	X			X		X	X
Spiral CT (non-contrast)				X		X *Optional*	X *Optional*
Completion Angiogram		X					
Magnified Branch Visualization		X					
Abdominal Ultrasound	X		X	X	X	X	X
Multiplanar Device Radiographs (X Ray)				X		X	X

[a] If subject is unable to return to the site for a follow-up visit, they may be contacted by telephone to evaluate the Modified Rankin Scale and Spinal Cord Ischemia Scale.

[b] For subjects suspected of having a stroke event within 30 days following the index endovascular procedure an additional mRS score should be completed at 90 days following the suspected stroke event but no greater than 120 days post index endovascular procedure.

[c] NIH Stroke Scale should be performed for any subject suspected of having a stroke event that undergoes the treating site's stroke protocol during the study interval from the initiation of the index endovascular procedure until discharge. The scale should be performed as soon as possible after learning of the suspected event and again at the time of discharge.

[d] CTA of chest/abdomen/pelvis at Screening. CTA of abdomen and pelvis at all follow-up visits, except for Secondary Study Arm Subjects who must have a CTA of chest/abdomen/pelvis at all visits. MRA may be used in place of CTA during follow-up if the Subject is contraindicated for CTA.

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 in **Table 5**.

Table 5: Follow-up Visit Ideal and Analysis Window Definitions

Follow-up Visit	Ideal Window (days)	Analysis Window (days)
Procedure	0	0
Discharge*	Before hospital discharge	N / A
Post-Procedure	Not required	1-14
1 Month	23-44	15-59
3 Month	76-104	60-126
6 Months	150-210	127-242
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

*Follow-up visit is categorized as "Discharge" through initial hospitalization, regardless of length.

4.3 Data and Safety Monitoring Board

See Section 9.3 of the protocol for information on the Data and Safety Monitoring Board.

4.4 Clinical Event Committee

See Section 9.4 of the protocol for information on the Clinical Events Committee.

4.5 Site Enrollment Restrictions

The maximum number of implanted subjects that may be implanted at a single site is as follows:

- Primary Study Arm Subjects: 15 subjects
  - Continued Access + Primary Study Arm: 21 subjects (this is a temporary site maximum which will be lifted after the first 27 subjects have enrolled in Continued Access)
- Secondary Study Arm Subjects: No maximum

4.6 Core Lab

See Section 6.4 of the protocol for information on the Core Lab.

4.7 Handling of Missing Dates

Imputation of dates is not planned for Primary Analysis. However, if it becomes necessary for an analysis of adverse events, the earliest possible date will be used, given the information available. If the month and year are provided, but the day is missing, then the first day of the month will be imputed. If only the year is provided, then the first day of the first month will be imputed, or the first day after procedure imputed if the first day of the year is prior to the procedure.

5. Statistical Analyses

5.1 Analysis Populations

The following populations will be used in various analyses of the data collected in the AAA 17-01 study:

1. All Enrolled Subjects - This population will consist of all enrolled Subjects. A patient is considered enrolled into the study once the Main informed consent has been signed and dated.
2. All Enrolled and Implanted Subjects - This population will consist of all enrolled and implanted Subjects. A patient is considered enrolled into the study once the Main informed consent has been signed and dated, and successfully implanted with the study device (TAMBE in the primary arm, CTAG + TAMBE in the secondary arm).
3. Uncomplicated Technical Success Eligible Population (each study arm) [Per protocol population] - This population will consist of enrolled and implanted Subjects with a follow-up visit at or after 30 days following initial TAMBE Device implant procedure. Additionally, any Subjects with an eligible technical success event, as defined in **Section 2.3.1**, even if they did not complete a follow-up visit at or after 30 days following initial procedure, will be included.
4. Clinically Significant Reintervention / Lesion Related Mortality Population (each study arm) - This population will consist of enrolled and implanted Subjects that have completed the 12 month analysis window. Additionally, any Subjects with an eligible clinically significant reintervention event, as defined in **Section 2.3.1**, even if they did not complete the necessary follow-up visit or imaging to otherwise be included in the population, will be included.
5. Secondary Effectiveness Populations (each study arm, each endpoint) - These populations will consist of enrolled Subjects with an evaluable result for the specific variable.
6. Reduced Profile VBX Population – This population will consist of the subjects in the Continued Access Phase who had been implanted with at least one reduced profile VBX device.

5.2 Endpoint Variables

The sources for the endpoint variables can be found in **Table 1**,**Table 2**, and **Table 3** in **Section 2.3.1** and **Section 2.3.2.**

5.3 Timing of Analyses

The Uncomplicated Technical Success / Procedural Safety endpoint will be analyzed after all Subjects eligible for the Primary Arm Uncomplicated Technical Success / Procedural Safety Eligible Population have completed a follow-up visit in the 12 month follow-up window and have been on the study for 90 days.

The Clinically Significant Reintervention endpoint will be analyzed after all Subjects eligible for the Primary Arm Clinically Significant Reintervention Eligible Population have completed a follow-up visit in the 12 month window.

The primary safety endpoint will be analyzed in the Primary Study arm during the effectiveness analysis.

The Primary and Secondary Study arms will be treated independently from each other, with the secondary study arm limited to descriptive analysis.

The Sponsor will collect data that comprise the secondary endpoints throughout all study follow-up (5 years), as appropriate, in addition to their specified analysis times (see **Section 4.2**). For endpoint events that rely on CEC adjudication, site reported data will be used to assess endpoints after the 12 month analysis period.

Following accrual of the initial 102 study subjects into the Core Clinical Investigation, up to 65 additional study subjects will be enrolled and implanted to allow for Continued Access to the device after the original enrollment is complete. The initial and additional subjects will be evaluated per the Inclusion / Exclusion criteria and will employ the same follow-up schedule. All statistical inference for the PMA submission will be based on the initial 102 subjects. Data from subjects enrolled in the Continued Access cohort will be reported separately but may be pooled with the initial data for subsequent follow-up reports.

Analyses of the reduced profile VBX Device will be completed once a minimum of 10 subjects (of the Continued Access phase) are enrolled and implanted with reduced profile VBX Device and followed through 30 days

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 Uncomplicated Technical Success and Clinically Significant Reintervention hypotheses in the Primary Study Arm. The null hypothesis for each endpoint will be rejected if the lower bounds of the 95% confidence interval exceeds the corresponding 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.

Primary and Secondary Endpoints will be summarized in the Secondary Study Arm, but no hypotheses tests will be performed.

All events must meet the protocol definition.

5.4.1 Uncomplicated Technical Success / Procedural Safety Endpoint Events

Uncomplicated Technical Success endpoint events in each study arm will be computed as all enrolled Subjects experiencing an event meeting the definition in **Section 2.3.1.**

5.4.2 Clinically Significant Reintervention / Lesion Related Mortality Events Endpoint Events

Clinically Significant Reintervention endpoint events in each study arm will consist of all enrolled Subjects experiencing an event meeting the definition in **Section 2.3.1.**

5.5 Adverse Events

The definition for Anticipated Adverse Events is given in Section 9.1 of the protocol. Section 9.1.1 describes the assessment of AE relationships, Section 9.1.2 describes determination of seriousness, and Section 9.1.3 describes their reporting and coding.

5.6 [redacted]

5.6.1 [redacted]

5.6.2 [redacted]

[redacted]

[redacted]

6. 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.

7. Analysis Specifications

7.1 [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. Verification levels are explained in MD111325 Clinical Affairs Biostatistics Analysis Specification and Programming.

8. Data Sets, Tables, Figures, and Listings

This section includes a list of the minimal planned statistical outputs, including tables, listings and figures which are to be created for the regulatory reports defined in the protocol. A different selection of tables, listings, and figures can be created for all other reporting efforts (DSMB, Annual Report, etc.) as decided necessary. Dataset names and descriptions may also be included.

8.1 [redacted]

- [redacted]

[redacted]

[redacted]

[redacted]

9. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

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