“Real-World Data Collection of the GORE® [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries”

05 Oct 2022

NCT05143138

PRINCIPAL INVESTIGATOR SIGNATURE PAGE

Principal Investigator: Please complete the information below. If instructed by W. L. Gore & Associates, Inc., (Gore), please sign and date the bottom of the page and return the original to the Gore registry contact. Retain a copy with the protocol at the registry site in the regulatory binder.

Device: [redacted]

Title: "Real-World Data Collection of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries"

Protocol Number: [redacted] 21-04
Protocol Date: 05 Oct 2022

I, the undersigned, have read and understood the specified protocol and agree with the contents. The protocol and any additional information provided by the sponsor will serve as a basis for conduct of the registry.

Name and Title (print): _____

Address: _____
_____
_____

Phone: _____

Signature: _____ **Date**: _____

Real-World Data Collection of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries

Protocol number: [redacted] 21-04

Protocol date: 05 Oct 2022

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

PROTOCOL SUMMARY

Registry Title	Real-World Data Collection of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries
Protocol Number	[redacted] 21-04
Registry Device	[redacted]
Sponsor	W. L. Gore & Associates, Inc. [redacted]
Registry Design	Multicenter, single-arm retrospective and prospective registry
Local Representative	Gore Authorized Representative W. L. Gore & Associates B.V. [redacted]
Registry Objective	The primary objective is to confirm the clinical performance of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries. The secondary objective is to confirm safety of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries.
Registry Endpoint(s)	Target vessel patency (patient level) at 12 months
Subject Population	Patients treated with the [redacted] as a Bridging Stent in conjunction with a branched/fenestrated stent-graft to allow endovascular aneurysm repair
Inclusion Criteria	1. Patients treated with the [redacted] as a Bridging Stent in conjunction with a branched/fenestrated stent-graft to facilitate endovascular aneurysm repair from 31 December 2021 until 01 January 2017 2. Age ≥18 years at the time of implant

<table>
<tr><td></td><td>3. An Informed Consent Form (ICF) signed by subject or next of kin/legal representative (for deceased patients at registry entry, unless a waiver was granted), according to local regulations.</td></tr>
<tr><td>Exclusion Criteria</td><td>1. Patient treated for ruptured aneurysm or who were otherwise hemodynamically unstable at the time of the procedure
2. Patient treated for acute or subacute dissection, <90 days from onset of symptoms
3. Patient treated using physician-modified endovascular grafts
4. Patient intended to be treated with chimney, periscope, octopus, sandwich technique per the pre treatment case plan.
5. At the time of treatment, patient had known coagulation disorders including hypercoagulability that were not amenable to treatment
6. Patient was pregnant at the time of treatment.
7. Participation in another drug or device investigational study within one year of device implant, that can confound the registry endpoints.
8. Patient had known or suspected systemic infection (including treatment for mycotic aneurysm) at the time of implant.</td></tr>
<tr><td>Number of Subjects</td><td><table>
<tr><th>Subject Cohort</th><th>Number patients</th><th>Caps per site (patient)</th></tr>
<tr><td>Fenestrated repair (FEVAR)</td><td>100</td><td>First cap 10% (10 patients)
Second and max Cap 30% (30 patients)</td></tr>
<tr><td>Branched repair (BEVAR)</td><td>120</td><td>First cap 10% (12 patients)
Second and max Cap 30% (36 patients)</td></tr>
<tr><td>Fenestrated-branched repair</td><td>Up to 40</td><td>N.A.</td></tr>
</table></td></tr>
<tr><td>Number of Sites</td><td>Up to 15 sites in Europe</td></tr>
<tr><td>Coordinating PI</td><td>[redacted]
Contact details and professional position are kept separately from this protocol</td></tr>
<tr><td>Registry Duration</td><td>Time to complete enrollment: 8 months, all subjects are enrolled retrospectively
Follow-up time: FU data collection up to 5 years. Part of the FU will be prospective.
Total registry duration: 5.5 years</td></tr>
</table>

Additional Information	**Contract Research Organization (CRO):** [redacted] **Electronic Data Capture System:** [redacted] **Core Lab:** [redacted] **Imaging Transfer:** [redacted]

LIST OF ABBREVIATIONS

AE	Adverse Event
ADE	Adverse Device Effect
ASA	American Society of Anesthesiologists
BEVAR	Branched endovascular aneurysm repair
CAAA	Complex abdominal aortic aneurysms
CABG	Coronary Artery Bypass Graft
CAD	Coronary Artery Disease
CBC	Complete Blood Count
CDMS	Clinical Data Management System
CE	Conformité Européenne
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CIP	Clinical Investigation Plan
cm	Centimeters
CRF	Case Report Form
CRO	Contract Research Organization
CT	Computed Tomography
CTA	Computed Tomographic Angiography
DTA	Descending Thoracic Aortic
EC	Ethics Committee
EDC	Electronic Data Capture
eCRF	Electronic Case Report Form
ePTFE	Expanded Polytetrafluoroethylene
ESVS	European Society for Vascular Surgery
EU	European Union
FEVAR	Fenestrated endovascular aneurysm repair
FDA	Food and Drug Administration (United States)
Fr	French (sizing)
GCP	Good Clinical Practice
GIS	Gore Imaging Sciences
HE	Health Economics
ICF	Informed Consent Form
ICH	International Conference on Harmonization

IFU	Instructions for Use
LAR	Legal Authorized Representative
LSA	Left Subclavian Artery
MDD	Medical Devices Directive
MDR	Medical Devices Regulation
MI	Myocardial Infarction
mm	Millimeters
MRI	Magnetic Resonance Imaging
OMA	Office of Medical Affairs (W. L. Gore & Associates, Inc.)
PG	Performance Goal
PHI	Protected Health Information
PI	Principal Investigator
SAE	Serious Adverse Event
SVS	Society of Vascular Surgery
TAAA	Thoraco-Abdominal Aortic Aneurysms
TIA	Transient Ischemic Attack
USADE	Unanticipated Serious Adverse Device Effect

DEFINITIONS

Adverse Event: Untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including an abnormal laboratory finding) in subjects, users, or other persons, whether or not related to the investigational medical device whether anticipated or unanticipated. This definition includes events related to the investigational medical device and events related to the procedures involved

Adverse Device Effect: Adverse event related to the use of an investigational medical device

Clinical Investigation Plan: A set of documents that describes the rationale, objectives, design and proposed analysis, methodology, monitoring, and the plan for the conduct of a clinical investigation. These documents may include the protocol, monitoring plans, and statistical analysis plans.

Device Deficiency: Any inadequacy in the identity, quality, durability, reliability, safety, or performance of an investigational device, including malfunction, use errors, or inadequacy in information supplied by the manufacturer.

Enrollment: A patient is considered enrolled into the registry once informed consent has been signed and dated or consent is waived.

Registry Device: The medical device being assessed for safety or performance in this registry. May also be referred to as registry device. This includes medical devices already on the market that are being evaluated for new intended uses, new populations, new materials, or design changes.

Serious Adverse Event: Any adverse event that led to any of the following:

(a) death

(b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:

(i) life-threatening illness or injury,

(ii) permanent impairment of a body structure or a body function including chronic diseases,

(iii) in-patient or prolonged hospitalization,

(iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function

(c) fetal distress, fetal death, or a congenital abnormality, or birth defect including physical or mental impairment

Defined in more detail in section 9.1.2.

Serious Adverse Device Effect: An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

Serious Health Threat: Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons.

Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree or incidence in the investigational plan or application (including

a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unanticipated Serious Adverse Device Effect: Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the protocol and IFU.

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1. Introduction

1.1. Disease

Complex abdominal aortic aneurysms (CAAA) and thoraco-abdominal (TAAA) are those that affect the visceral aortic branch vessels (including the renal, the celiac trunk and the superior and inferior mesenteric arteries).[1] CAAA (including short-necked infrarenal juxtarenal, paravisceral and suprarenal aneurysms) are defined as aneurysms that involve the renal or mesenteric arteries and extend up to the level of the celiac axis or diaphragmatic hiatus but do not extend into the thoracic aorta.[2] Aneurysms extending proximal to the renal arteries which involve variable extent of the thoracic aorta are referred to as TAAA which were classified by Crawford-Safi based on the extent of surgical repair required. ESVS guidelines[3] provide anatomic descriptions which are included in Table 1.

Table 1. TAAA Classification per ESVS Treatment Guidelines

TAAA Type	Definition[3]
Type I	Start at the level of the left subclavian artery, or at least proximal to the level of the sixth vertebra (T6) and affect the entire DTA, involve the visceral arteries and end at the renal arteries. The aneurysm can involve the origin of the LSA or even involve the distal aortic arch.
Type II	Start at the same level as a type I, but involve the DTA and the entire abdominal aorta
Type III	Start more distal than type II aneurysms, usually at the level of T6, and extend distally as in a type II.
Type IV	Start at the level of the diaphragm and involve the entire abdominal aorta, with or without extension to the iliac arteries.

1.2. Historical Treatments

CAAA and TAAA involving the visceral segment may be treated by open surgical repair specific to the type of aneurysms or a variety of endovascular techniques. The purpose of this registry is to assess the utility of the [redacted] as a bridging stent when used in conjunction with a branched or fenestrated stent graft. Therefore, this review will focus on the devices that are used in this application.

In early experience with fenestrated grafts, bare metal stents were commonly employed primarily to maintain alignment of the fenestration with the target vessel. As an example, the Cook Zenith® fenestrated graft study reported a mixed usage of bare metal and covered stents in the bridging application.[4] In this report, loss of patency was higher in vessels treated with bare metal stents, although this was not statistically significant. Over time, balloon expandable covered stents have become the preferred option for FEVAR. More recently, Farivar and colleagues published results with a variety of devices and conclude that the choice of balloon expandable covered stent has no effect on branch durability in FEVAR procedures.[5]

In BEVAR procedures, a covered bridging stent is generally selected given the need to exclude the aneurysm from circulation while still maintaining perfusion of the target vessel. Mastracci and colleagues[6] performed an analysis of outcomes in branched aortic repair and were unable to demonstrate any difference in occlusion or reintervention between balloon-expandable and self-expandable covered stents.

The successful usage of the [redacted] has been reported in several publications involving FEVAR and BEVAR procedures[7-11], which suggests that this device may offer a reasonable option as a bridging stent in these applications.

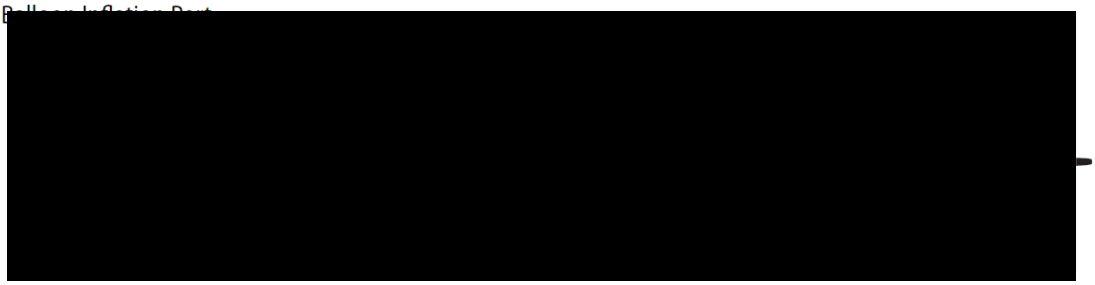
1.3. Registry Device Description

[redacted] The design, device sizes, and characteristics permit the use of the device in multiple pathologies.

[redacted]

[redacted]

[redacted]



[redacted]

1.4. Pre-clinical Data

Gore has performed the following pre-clinical testing on the [redacted]

1.5. Clinical Data

[redacted]

More detailed device information can be found in the Instructions for Use (IFU)

2. Registry Objectives

2.1. Primary Objective(s)

The primary objective is to confirm the clinical performance of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms Involving the Renal-Mesenteric Arteries.

2.2. Secondary Objective(s)

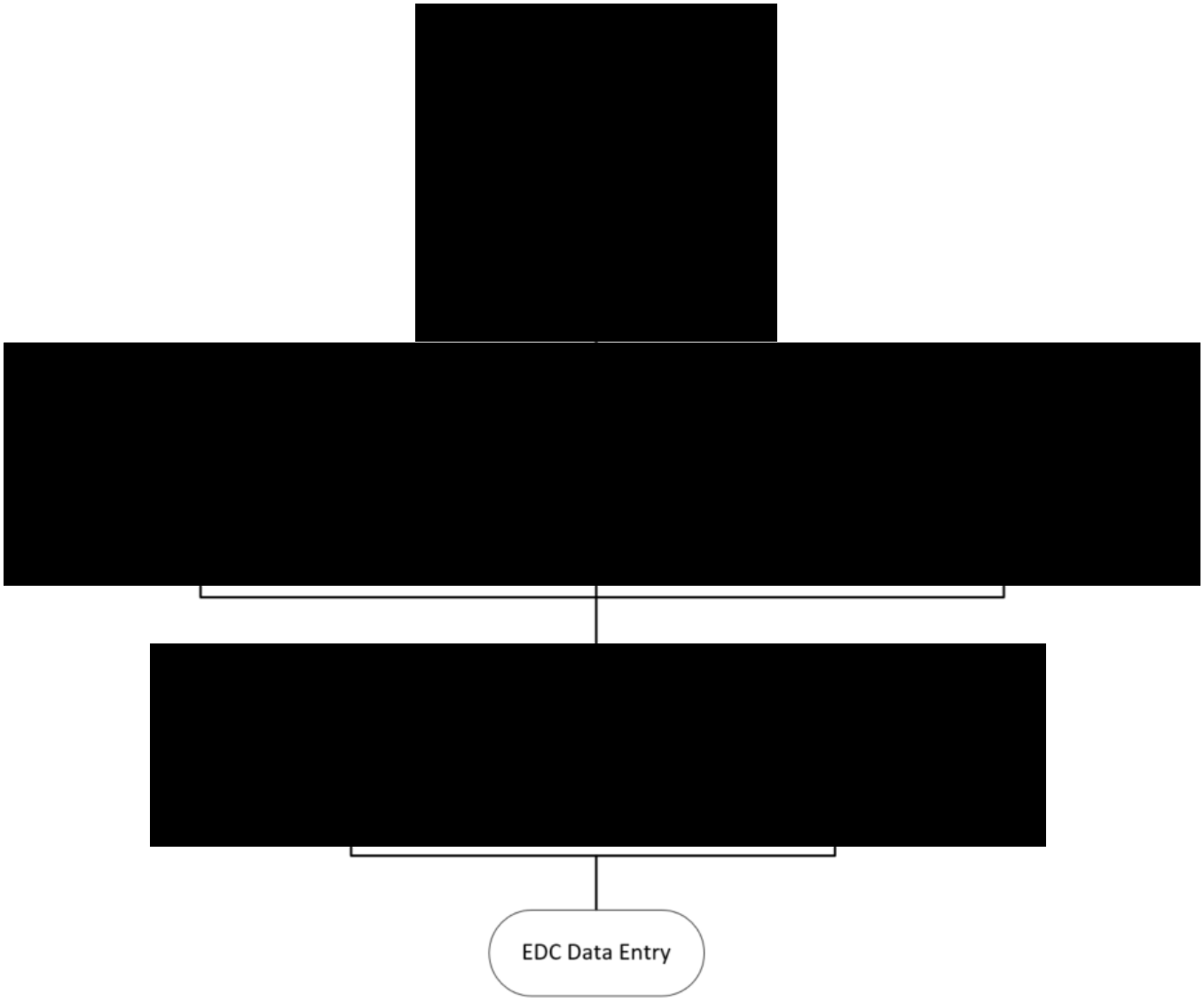
The secondary objective is to confirm safety of the [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms involving the Renal-Mesenteric Arteries.

2.3. Health Economic Data Analysis

A Health Economic analysis will be performed using clinical registry data. The objective of the Health Economic analysis is to understand the value of the treatment(s) studied during the period of the registry.

3. Registry Design

3.1. Registry Design Schema



3.2. Description of Registry Design

This multicenter, single-arm retrospective and prospective registry is being conducted to confirm the clinical performance and safety of [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms Involving the Renal-Mesenteric Arteries.

A single arm design was chosen as the clinical application does not readily lend to randomization due to involvement of multiple vessels and variability with respect to the main body design.

A retrospective and prospective registry was determined to be suitable observational study design to reliably answer the research question, based on consistency of device design, procedures, clinical results available and operative techniques.

Up to 15 sites in Europe will be required to enroll a minimum of 220 patients that have had treatment with [redacted] when used as a Bridging Stent with Branched and Fenestrated Endografts in the Treatment of Aortic Aneurysms Involving the Renal-Mesenteric Arteries.

Each site cannot contribute to more than 10% of the total patient for each cohort without sponsor approval, with a maximum of 30% of total enrollment for a single site. See section 4.1 for more details.

The Sponsor or designee will maintain an updated list of all principal investigators, site names, and addresses. This list shall be kept separately from this protocol.

Subjects may be enrolled when all inclusion and no exclusion criteria are met as specified in section 4.2. Patients are enrolled into the registry when they provide consent or consent is waived and meet all inclusion and exclusion criteria.

Subjects' medical records will be reviewed by the investigator and specific data will be collected retrospectively and prospectively for up to 5 years of follow-up from the index procedure.

3.3. Management of potential confounding factors / bias

Bias will be controlled by strict adherence to the registry protocol. Sites will be monitored for compliance with registry protocol, including subject eligibility criteria, as allowed by EC regulations. In order to minimize selection bias, it is mandatory that the enrollment of patients will be consecutive in nature based on the date of the index procedure. Gore has put in place quality control to ensure that no selection bias is applied by the site during patient screening, please see section 5.5 for more details.

The registry is meant to retrospectively and prospectively collect data for reporting as well as evaluate "real world" experience of clinical practice and patient outcomes during treatment and throughout follow-up extending up to 5 years. Patient selection, diagnostic imaging and treatment interventions will be determined by physicians based on this protocol and clinical practice standards.

It is well known that excluding treated patients who are deceased or not reachable at the time of the inclusion due lack of informed consent can generate an important selection bias in retrospective study and is likely to seriously prevent the achievement of the research objectives. Therefore, for patients, who are deceased or not reachable at the time of the inclusion, the consent can be waived, signed by next of kin/legal representative, according to local regulations.

Refer to section 5.3.1 regarding the waived process.

3.4. Registry Endpoint(s)

3.4.1. Definitions

Outcome	Definition per SVS reporting Standards
Technical Success Related Outcomes	
Target Vessel Technical Success	Successful catheterization and [redacted] placement in all intended target vessels. For this registry, technical success will be reported for the overall procedure and specifically for the vessels targeted for treatment with the [redacted]
Primary Technical Success (Total Endovascular Procedure)	A modified technical success definition, requiring the following: 1. Successful side branch catheterization and placement of bridging stents with restoration and maintenance of flow in all intended target vessels 2. Patency of all aortic modular stent graft components and intended side branch components 3. Absence of type I or type III endoleaks at completion angiography that extends beyond 30 days by confirmatory imaging (CTA, magnetic resonance angiography [MRA], or duplex ultrasound)
Vessel Patency Related Outcomes	
Primary Patency (Primary Endpoint)	Uninterrupted patency with no occlusion or procedure performed to maintain patency on the [redacted]t or native target vessel. Interventions intended to treat endoleak or stent disconnection do not count as loss of primary patency.
Primary Assisted Patency	Endovascular intervention performed to maintain patency in the presence of a stenosis before occlusion

Secondary Patency	Endovascular restoration of patency after occlusion of the side branch, stent, or stent graft has already occurred. Conversion to bypass or inability to treat by endovascular means defines loss of secondary patency
Occlusion	Objective documentation by angiography, computed tomography, or ultrasound of complete stent occlusion with or without minimal flow into a targeted vessel
Stenosis	Objective documentation by angiography, computed tomography, or ultrasound of stenosis intra-stent or into a targeted vessel
Kink	Objective documentation by angiography, computed tomography, or ultrasound of kink in the stented or native segment of a targeted vessel
Other Outcomes	
Intraprocedural complications	Any vessel perforation, dissection, or occlusion during target vessel stenting
Reintervention	Any repeated vascular or nonvascular procedure related to the index procedure Reintervention will be adjudicated as major or minor based on the following Major: deployment of proximal or distal aortic or iliac extensions, removal of the device, use of thrombectomy or thrombolysis, and any major open surgical procedure. Minor: endovascular procedures (percutaneous transluminal angioplasty, atherectomy, stenting) without thrombectomy or thrombolysis, interventions to treat branch vessel stenosis, interventions to treat type II endoleak or branch-related endoleaks, and minor surgical revisions (patch angioplasty) of the access vessels. Each reintervention will be adjudicated as related to a [redacted]-treated branch vessel component, related to a non-[redacted]-treated branch vessel component, or related to main body component(s), if possible.
Target vessel instability	Death or rupture related to side branch complication (e.g., endoleak) or reintervention to treat a branch-related complication, including endoleak, disconnection, kink, stenosis, occlusion, or rupture

Aneurysm-related mortality	Any death that occurs within the first 30 days or any death that results from aneurysm rupture, aorta-related complications (eg, infection, occlusion, dissection, hematoma), or a complication of a secondary intervention
Major Adverse Events (MAEs)	All-cause mortality Myocardial infarction (MI): MI resulting in severe hemodynamic dysfunction necessitating resuscitation, cardiac arrest, or fatal outcome. Respiratory failure requiring prolonged (>24 hours from anticipated) mechanical ventilation or reintubation Any renal function deterioration according to the RIFLE classification system. Bowel ischemia requiring surgical resection or not resolving with medical therapy Permanent paraplegia (any grade 3 A-C spinal cord injury) in a patient who is no ambulatory. Any major stroke defined according to National Institutes of Health Stroke Scale (NIHSS) or equivalent.

3.4.2. Primary Endpoints

- Primary Performance Outcome: Target vessel patency (patient level) at 12 months

3.4.3. Secondary Endpoints

Secondary performance outcomes

- Reintervention (total and reintervention that can be attributed to branches originally treated with the [redacted]) at 12 months and annually through 5 years post-implant
- Target Vessel Technical Success
- Primary Technical Success (Total Endovascular Procedure)
- Target vessel instability at 12 months and annually through 5 years post-implant
- Target vessel patency, patient level, annually from 2-5 years post-implant (extended primary endpoint)
- Target vessel patency, vessel level analysis, annually from procedure to 5 years post-implant

Secondary safety outcomes

- Aneurysm-related mortality at 12 months and annually through 5 years post-implant
- MAEs at 30 days

4. Registry Population

4.1. Description of Population

The registry population will consist of patients that have had treatment with [redacted] and that meet the registry eligibility criteria.

Subject Cohort	Treatment period	FU period after index procedure* (years)	Number patients	Caps per site** (patient)
Fenestrated repair (FEVAR)	From July 2021 to Jan 2017	5	100	First cap 10% (10 patients) Second and max cap 30% (30 patients)
Branched repair (BEVAR)	From July 2021 to Jan 2017	5	120	First cap 10% (12 patients) Second and max cap 30% (36 patients)
Fenestrated-branched repair***	From July 2021 to Jan 2017	5	Up to 40	N.A.

* Subject who died before the end of FU period will be not excluded from the registry.

** for FEVAR and BEVAR cohorts an enrollment cap is fixed at 10% of the total patients without sponsor approval. With sponsor approval, a single site may enroll a maximum of 30% of total patients.

***Hypothesis testing will be performed on the FEVAR and BEVAR cohort only.

Target for hypothesis testing is to have 220 subjects among FEVAR and BEVAR only subjects. The registry also accounts for mixed cases that can be enrolled according to consecutive screening procedure, as described in section 5.5

Site's registry staff will review patients' medical records to identify eligible patients for this retrospective and prospective data collection. The registry has been designed with standard eligibility criteria to enroll subjects for which the registry device has been intended to treat. Only patients who meet all of the inclusion criteria and none of the exclusion criteria will be included in the registry.

Considering the nature of the patient's disease, elderly patients (≥ 65 years old) can represent the majority of subjects enrolled in this registry. This population can include patients with cognitive disorder or severe dementia.

According to EU regulation, elderly patients are considered vulnerable population. However, considering the retrospective nature of the registry, the patients have already been treated at the time of the inclusion, therefore there are not additional risks for this vulnerable population (please see risk assessment at (section 9) to be included in this registry.

4.2. Inclusion Criteria

The Inclusion Criteria reflects the potential broad application of the device as evaluated by the medical judgement of the implanting physician. Inclusion Criteria will be evaluated at the time of initial identification as part of the retrospective device-use search using the patient health status at the time of the index procedure.

1. Patients treated with the [redacted] as a Bridging Stent in conjunction with a branched/fenestrated stent graft to allow endovascular aneurysm repair from 31 December 2021 until 01 January 2017
2. Age ≥18 years at the time of implant
3. Provision of informed consent by the patient or next of kin/legal representative (for deceased patients at registry entry, unless a waiver was granted), according to local regulations.

4.3. Exclusion Criteria

1. Patient treated for ruptured aneurysm or who were otherwise hemodynamically unstable at the time of the procedure
2. Patient treated for acute or sub-acute dissection, <90 days from onset of symptoms
3. Patient treated using physician-modified endovascular grafts
4. Patient intended to be treated with chimney, periscope, octopus, sandwich technique per the pre-treatment case plan
5. At the time of treatment, patient had known coagulation disorders including hypercoagulability that were not amenable to treatment
6. Patient was pregnant at the time of treatment.
7. Participation in another drug or device investigational study within one year of device implant, that can confound the registry endpoints.
8. Patient had known or suspected systemic infection (including treatment for mycotic aneurysm) at the time of implant.

5. Registry Procedures / Evaluations

No product or procedure-related training is required, the registry is designed to retrospectively collect pseudo-anonymized data on demographic (including medical history), procedure, clinical follow-up, and device characteristic from the patient's medical record.

Similarly, for follow-up data that will be collected prospectively, the registry will not require the use of any procedure and / or test and / or medical device different from those required by routine clinical practice for following up the investigated pathologies. Each site will be responsible for using and maintaining the equipment and medical devices in accordance with the manufacturer's directions and their institutional practices.

The sponsor will not impose requirements that limit health care professionals from exercising their best medical judgment for treatment. Therefore, follow-up modalities will be determined by physicians based on clinical practice standards.

For this registry it is expected that the sites will follow this protocol to ensure scientifically sound evaluation of outcomes. There are no additional, known or foreseeable factors that may compromise the outcome of the registry or the interpretation of results; please refer to section 3.3 regarding minimization of bias.

5.1. Registry Procedures and Evaluation Schema

5.2. Schedule of Events

[redacted]

[1] Available information used in case planning (e.g. diagrams, imaging) will be requested as part of registry documentation

[2] Available imaging performed per the site standard of care for complex EVAR procedures and follow-up. This may include angiography, echocardiography, X-Ray, computed tomography and/or magnetic resonance. Any available imaging performed (fully anonymized) can be requested as part of registry documentation.

[3] Medication collected: Antiplatelet and anticoagulant therapy

[4] The start of the prospective phase may change from subject to subject depending on the treatment date.

[5] collection of any possible re-intervention data

[6] Lab result will be collected if available, and can include, RBC, WBC, platelet, Creatinine, eGFR

5.3. Informed Consent Process

For the inclusion of patients in the registry, the investigator should review all inclusion/exclusion criteria and, in the case of including patients who are alive and reachable at the site, the patient will be required to sign the Ethics Committee approved Informed Consent Form (ICF) before enrolment in the registry.

As this registry is retrospective and considering the nature of patient's disease, some patients may [redacted].

If, during the course of the registry, patients who were not previously reachable come back to the clinical site for a visit, the investigator is expected to collect informed consent from those patients.

To protect patient privacy, patient-identifiable information (e.g., name, initials, complete birth date, and race) will not be collected in the registry clinical data management system.

The informed consent form will include emergency contact details for any concerns. The case history (i.e., source documents / subject chart) for each subject shall document that such informed consent was obtained, [redacted]

The EC approved consent form will be signed and personally dated by the subject or next of kin/legal representative (for deceased patients at registry entry, unless a waiver was granted), according to local regulations and the person who conducted the informed consent discussion. The original signed informed consent form will be retained in the subject records. A copy of the signed informed consent document will be given to the subject for their records.

5.3.1. [redacted]

Considering the low risk (see section 8, Risk Assessment) of this retrospective registry and the absence of registry-specific procedures for the patient, t[redacted] Specific procedures to ensure adequate documentation of [redacted] informed consent process, in accordance with regulation and best clinical practice, will be provided to the investigators in a separate document.

5.3.2. Vulnerable Populations

Vulnerable population is described in section 4.1

In case the patient is unable to make the decision to participate in this registry, Informed consent should be signed by next of kin/legal representative (LAR), according to local regulations. In such cases, the subject shall also be informed about the registry within his/her ability to understand and the subject should sign and personally date the written informed consent if capable.

5.3.3. Emergent Cases

Not applicable due to retrospective nature of the registry

5.4. Pre-Screening

Site are expected to perform a search of patients treated with [redacted] as a Bridging Stent in conjunction with a branched/fenestrated stent-graft within the hospital database following the site initiation performed by Gore. Upon site activation, [redacted]

Screening will be divided in two phases:

[redacted]

The research results will be recorded in the Pre-screening list based on patient's date of index procedure in reverse chronological order (from newest to oldest patient treated).

[redacted]

The pre-screening list produced during phase one and two must be maintained at the site in order to document the reasons for exclusion for any patient preventing bias of the data. This list cannot be sent to Gore/other external individuals (CRO) but is available at the site in the registry binder for audit/inspection purposes.

5.5. Enrollment

Patient enrollment should be consecutive,and will occur according to paragraph 5.4 .

From the pre-screening list (sorted by treatment date), the site should review patients against inclusion and exclusion criteria, then check whether the patients are still alive and reachable in order to obtain consent. The patient is considered enrolled when informed consent is obtained [redacted] (LAR), according to local regulations

In order to minimize selection bias and to prove that patients have been screened in consecutive fashion, all patients, present in the pre-screening list, who will undergo inclusion/exclusion criteria assessment, [redacted] until the site reaches the max cap of enrolled patients planned for this registry or until the cohort is completed.

If patient identified in the pre-screening list will not be enrolled, [redacted] no personal information is recorded. The investigators will identify additional subjects to be screened.

During the on-site monitoring visit, the monitor should review Subject Screening and Enrollment log against the subjects recorded in the EDC, in order to prove the enrolment occurred sequentially.

5.6. Screening

Formal screening will not be performed due to retrospective nature of this registry.

No screening procedures are performed, with exception of reviewing of the inclusion and exclusion criteria based on the information already present in the patient's medical record.

5.7. Screen Failure

For clarity, this registry defines screening failure as subjects from the pre-screening list who:

- do not meet Inclusion/Exclusion criteria.

- declined consent.

However, if after the collection of the consent, the subjects do not meet eligibility criteria, the primary reason for screen failure [redacted]. The subject will be excluded from the registry and a replacement subject may be enrolled in agreement with sponsor and investigator.

5.8. Randomization and or Blinding

No randomization or blinding is to be performed due to the confirmatory nature of the registry design.

5.9. Procedure

The registry procedures consist of two phases, retrospective phase and prospective phase.

The retrospective phase consists only of the collection of retrospective data (baseline, treatment and FU data) from the source documents available at the site from the time of the treatment until the enrollment date (ICF signature). It is expected that sites will provide pre and post treatment as well as treatment images for Core Lab review.

The prospective phase consists in collection of follow-up visits from the enrollment up to 5 years. The FU data collected prospectively can change from subject to subject depending on the index procedure date. Diagnostic imaging, treatment interventions, and follow up will be determined by physicians based on clinical practice standards.

5.10. Repeat Interventions

Reinterventions may be performed at the discretion of the principal investigator / sub-investigator to treat AEs. Any reinterventions performed will be documented on the CRF form. The components used as part of the reintervention, the date of the reintervention and the AEs leading to reintervention will also be documented on the CRF form.

5.11. Follow Up

All follow-up performed from the index procedure to the ICF signature will be collected retrospectively. FU data will be collected from the information already present in the medical chart.

From the date of the enrollment, all FU visits including any imaging, performed according to hospital standard of care, will be collected up to 5 years post index procedure.

In addition to in person visits, remote phone follow-up is also acceptable and clinical information obtained via phone can be collected.

For testing done at institutions different than the registry site, or in case no follow-up data are available, investigators should make any efforts to retrieve documentation from the patient or from other records/sources (e.g. hospital databases, family doctor, family members).

Subjects will continue to be followed by the site's standard of care after completion of the registry.

5.12. Subject Withdrawal from the Registry

A subject may withdraw from the registry at any time and should notify the investigator in this event. The investigator may also withdraw the subject from the registry at any time based on his / her medical judgment. The sponsor may retain and continue to use any data collected before the withdrawal of consent, if not explicitly requested otherwise by the subject.

If such withdrawal is due to problems related to the device safety or performance, the investigator shall ask for the subject's permission to follow his / her status / condition outside the registry.

During the prospective phase, patients may be considered withdrawn for any of the following:

- Death
- Voluntary withdrawal
- Investigator withdrawal
- Any other medical condition where evaluation of the [redacted] is not feasible (e.g., bypassed [redacted], explant of the device)

If the discontinuation is caused by the development or worsening of AEs, information on the AEs must also be recorded on the appropriate eCRF. All data generated prior to patient withdrawal will be maintained, and registry data will be used as appropriate.

If possible, an additional evaluation of the [redacted](s) is recommended prior to their withdrawal from the registry.

5.13. Subject Lost to Follow Up

Due to the observational nature of this Registry and the variability of real - world follow-up frequency, patients will be declared lost to follow-up according to site's standard modalities or at the end of the 5 years FU windows. Attempt to contact the subject or next of kin will be documented in the subject files.

5.14. Subject Registry Completion

A subject has completed the registry when he/she has reached the 5 years post treatment (+/- 1 month) and the visit has been properly recorded in the EDC. Any subject who does not complete these requirements due to voluntary withdrawal, physician withdrawal, death, or any other reason will be considered a withdrawal.

After subject registry completion the site standard of care will be continued.

5.15. Explant Procedures

The [redacted] may be explanted during a surgical procedure or as part of an autopsy. If this occur during the prospective phase of the registry sites are requested to return explanted devices to the sponsor for gross and histological evaluation. Prior to planned or potential device retrieval, contact the Gore Associate managing the registry to communicate that a specimen is being retrieved from a registry subject. A specimen shipping kit will be immediately sent to the site. The specimen kit provides specific packaging and handling instructions for the specimen and contains a shipping container.

In complex aortic procedures it is expected that more than one [redacted] can be implanted in the same subject, if the explanted device is the only one used in the subject then the subject will be discontinued, if other [redacted] remain implanted the subject will continue in the registry.

6. Registry Administration

6.1. Training

All Investigators involved in this registry must be trained on the protocol, EDC and Good Document Practice by Sponsor associates, designees, or another appropriately trained physician at the registry Site.

6.2. Monitoring

Site monitoring for this protocol will be provided by [redacted] who are independent from the investigational site(s). Monitoring oversight will be provided by the sponsor. The Principal Investigator will be accessible to the monitor and respond to questions during monitoring visits.

The site monitors are qualified by training and experience to oversee the progress of the registry at the site and will verify that the investigators and their staff understand and adhere to both the applicable regulatory requirements and the registry protocol. In addition, they may assist in resolution of any problems that may arise during the registry.

6.3. Site Initiation

Site initiation will be performed to verify that each investigator and his / her staff understands the protocol, applicable regulations, human subject protection requirements, and the investigator's obligations. This visit will confirm that required documentation with the appropriate approval is in place prior to subject enrollment.

The registry shall not begin until the sponsor has confirmed the required approval / favorable opinion from the EC or regulatory authority have been obtained. Site Initiation can be performed remotely (web-conference) if on-site visit is not possible.

6.4. Periodic Site Monitoring

Periodic site monitoring will occur as necessary to verify continuing adequacy of facilities and adherence to the registry protocol, Good Clinical Practices (GCPs), and applicable regulations and laws that pertain to the conduct of the registry. These activities will also review the Case Report Forms (CRFs) and source documentation, the timely submission of accurate records to the sponsor, and the maintenance of proper records. A report will be written following each site visit and a follow-up letter will be provided to the site with a summary of findings. Each site will also be visited on-site or remotely contacted at close-out to confirm that all documentation is complete.

The registry will employ a risk-based monitoring approach where data are centrally reviewed for logical context, completeness, and obvious outliers. Only specific critical data variables will be source verified during on-site visits. Informed consent documentation or documentation that [redacted], will be reviewed for all patients to verify that all patients agreed to registry participation or are amenable for waiver. Monitoring procedures and requirements will be documented in a clinical monitoring plan developed and maintained by Gore.

6.5. Device Accountability and Storage

Due to the nature of this registry, participating sites will have utilized their commercial contractual agreement with the Sponsor or designee for device shipping, storage, use and return. Implanted device part numbers will be collected on CRFs, if available.

6.6. Core Lab

Core Lab services for this registry will be provided by [redacted] as referenced in Table 2.

Table 2: Core Lab specifications

Core Lab Name	Core Lab Location	Type of Imaging Reviewed	Main Assessments	Timepoint
[redacted]	[redacted]	[redacted]	[redacted]	Pre-procedure, Post-procedure and annually

The Core Lab will perform assessments of imaging modalities according to objective process and standard procedures completed by trained and qualified personnel.

Medical imagery will be transmitted to the Core Lab using the secure, web portal functionality of the [redacted]. Imaging submitted through the portal will be stripped of personal health information and replaced with appropriate registry subject identifiers in automated, systemic fashion. Recipients will process received imaging according to their standard operating procedures or registry-specific processes. [redacted]

Additional imaging modalities, such as magnetic resonance, may be performed during the course of the registry as part of standard practice or in response to a clinical event. Gore may request these films to be submitted to aid in the understanding of an event or to support the conduct of an independent review committee such as a Clinical Events Committee (CEC). [redacted]

The site needs to upload the required imaging using [redacted], making sure that all PHI is redacted.

6.7. Protocol Deviations

The investigator/ sub-investigator must follow the protocol, except in the event of an immediate hazard(s) to a subject. The investigator must report those deviations and explanation immediately to the sponsor. The investigator will report the protocol deviation in accordance with the applicable regulations.

A protocol deviation is defined as any change, divergence, or departure from the registry design or procedures of a research protocol. The investigator is responsible for promptly recording and reporting protocol deviations to the sponsor and the reviewing EC per EC policy. The sponsor will determine the effect of the protocol deviation on the scientific soundness of the registry and subject safety and determine if additional reports or actions are required. Additional action may include site retraining, and / or site termination.

The investigator will not implement any changes to the protocol without first obtaining written agreement from the sponsor and documented approval from the EC, except in the event of an immediate hazard(s) to a subject. The investigator will document and report the protocol deviation in accordance with the applicable regulations. Protocol deviations will be analyzed by the sponsor and reported to regulatory authorities in accordance with applicable regulations.

The investigator will determine the cause and implement appropriate corrective and preventive actions to address significant noncompliance to the protocol.

6.8. Protocol Amendments

The protocol may be amended by the sponsor throughout the life of the registry, as result of new findings or advisement from the applicable regulatory body or advisory committee. The investigator will obtain EC approval on all amendments in a timely manner. The sponsor will confirm proper training of Investigator and site staff on all protocol amendments.

6.9. Access to Source Data / Documents

Source data are defined as all information necessary for the reconstruction and evaluation of the clinical investigation.

The investigator and site staff should maintain adequate and accurate source documents and registry records that include all pertinent observations on each registry subject including documentation of the type and location of source documents. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry and should be explained if necessary (e.g., via an audit trail).

Where copies of the original source documents or printouts are retained, these need to be signed and dated by a member of the registry team with a statement that it is a true reproduction of the original source.

The investigator or designee will clearly mark subject clinical records to indicate the subject is enrolled in this registry.

The investigator will keep all registry records and source data, available for inspection by the sponsor, sponsor's monitors, EC, and regulatory authorities.

6.10. Registry Records Retention

The investigator will maintain complete, accurate, and current registry records as required by applicable regulatory requirements. Records will be maintained during the registry and for a minimum of 15 years after the latter of the date on which the registry is terminated or completed, where completion is intended as the last follow-up visit of the last treated subject. In any event, registry records will not be disposed of, nor custody of the records transferred, without prior written sponsor approval.

Investigator records will include, but not be limited to:

- All correspondence with another investigator, an EC, the sponsor, a monitor, or regulatory authority, including required reports.
- Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records, including, for example, progress notes of the physician, the individual's hospital chart(s), and the nurses' notes. Such records shall include:
    - Documents evidencing informed consent. In case the consent is waived, a brief description of the circumstances justifying the failure to obtain the informed consent. The case history for each individual shall document that informed consent was obtained or waived prior to participation in the registry.

- All relevant observations, including records concerning adverse device effects (anticipated and unanticipated), the information and date and condition of each subject upon entering, and information about relevant previous medical history and the results of all diagnostic tests.
- A record of the exposure of each subject to the device, including the date and time of each use, and any other therapy.

- The protocol, any amendments, and documentation of any deviations from the protocol, including the dates and the reasons for such deviations.
- Any other records that regulatory authority require to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- A signed Investigator Agreement, if applicable
- Any other records as required by the regulatory authority, the EC, and the sponsor.

The investigator will prepare and submit the following reports:

- Protocol deviations shall be reported as described in section 6.7.
- Other: Any other reports as reasonably requested by the sponsor or required by regulatory authority.
- Withdrawal of EC approval: The investigator will report any withdrawal of approval within 5 working days after the investigator has been notified of the withdrawal"

6.11. Publication Plan

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a trials-registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry. The sponsor will register the registry and post results as required by applicable regional laws and regulations.

It is the intent of the sponsor that the multicenter results of this registry will be submitted for one or more publications (in a peer reviewed journal). A publications committee will be established to review the multicenter results and develop one or more publications at the completion of the registry. The timing of the multicenter publication may be dependent on regulatory submissions and approvals. Individual sites should coordinate requests for publication through the publications committee or the sponsor/Clinical Science Liaison.

6.12. Health Economics

The sponsor may use registry data to develop a better understanding of the impact that the device may have on clinical practice in order to meet anticipated business needs. With consent of the subject and approval of the supervising EC, billing information may be collected to aid in this evaluation.

7. Data Collection and Submission

The validated Clinical Data Management System (CDMS) for this registry will be provided by [redacted] The sponsor keeps a separate Clinical Data Management Plan (CMMP) describing the procedures for verification, validation, and security of the CDMS. The CDMP will describe and document procedures regarding data management processes for this registry.

7.1. Data Collection Methods

This registry will report clinical data using the [redacted] CDMS web-based application. 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 registry 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.

7.2. 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. Sponsor will perform periodic data reviews throughout the entire registry. Procedures and documentation for regular and ongoing data review are described in the Clinical Data Management Plan.

7.3. CRF Completion Schedule

All registry data are targeted to be entered into the appropriate eCRF within 10 days of enrollment for the retrospective phase and within 10 days of collection for the prospective phase, however, data outside this window will not be considered a protocol deviation. Pre-Screening information will be recorded for all subjects and will only consist in inclusion /exclusion criteria evaluation, and enrollment information. All subsequent data entry will only occur after collection of inform consent to participate in the registry.

8. Risk Assessment

Given the registry design, subjects would have been already treated at the time of enrollment, therefore there is no potential for physical risks to subjects during the retrospective phase of the registry. T[redacted]

There is a minimal risk of [redacted] since subject information will be collected and analyzed for the proposed registry. However, appropriate measures will be taken to minimize the risk as much as possible. All information entered into the central registry database will be de-identified. This registry will abide by all regulations related to protecting human subjects and protected health information (PHI).

A complete listing of the known risks associated with the [redacted] can be found the IFU.

8.1. Potential Risks

Potential risks were listed in the IFU available at the time of the implant, given the retrospective treatment it is expected that majority of risk are no more applicable because related to the implant procedure. Nevertheless, some device related risks could potentially still occur in the long term i.e (see section Hazards and Adverse Events from IFU):

- Side branch occlusion
- Thrombosis

- Infection

8.2. Minimization of Risks

- The sponsor has conducted risk management activities for the [redacted] according to ISO14971:2019. Risks remaining after the risk control measures have been implemented are acceptable and the effectiveness of these measures have been verified. The combined impact of the individual risks has been assessed and found to be acceptable. The benefit of the product has been assessed against the overall residual risk and determined that the medical benefit of the product outweighs the risk. The overall residual risk for this product is comparable to similar products. Therefore, overall residual risk has been evaluated for the [redacted] and has been deemed acceptable. All appropriate methods are in place to collect clinical information during the trial for the [redacted] All risks related to the design, manufacturing and usability of the medical device have been reduced as far as possible.
- The sponsor has performed qualification testing on the device and device components and appropriate quality control measures have been implemented into production. Investigators will be selected who are knowledgeable and experienced in endovascular procedures.
- The site investigator, sub-investigators, study coordinator(s) or designee at each site will be trained to the protocol and subject follow-up requirements.
- Protocol inclusion / exclusion criteria and follow-up schedules are designed to select appropriate subjects and identify potential complications early.
- Safety and efficacy findings during the registry will be shared with the site investigators to aid understanding of the device and potential complications associated with its use.
- Possible interactions with concomitant medical treatments are not expected as such treatment will be consistent with best medical practices and institutional standards.

  The sponsor will promptly notify the investigator and regulatory authorities of findings that could affect the safety of subjects, impact the conduct of the registry, or alter the IRB / EC's approval to continue the registry.

8.3. Summary of Expected Benefits

Participation in this observational registry is not expected to provide any direct benefits to participating patients. However, the data collected during the registry will foster a better understanding of the performance of the registry device.

8.4. Risk-to-Benefit Rationale

The registry will not require the use of any procedure/follow-up and / or test and / or device different from those required by routine clinical practice for the treated conditions, therefore enrolled patients will not be exposed to additional risks as compared to routine clinical practice.

The clinical data supports an appropriate performance and safety profile and risk-benefit ratio, for the [redacted] when used as intended, and the potential benefits offered by the [redacted] outweigh the identified potential risks.

9. Adverse Events and Safety Monitoring

9.1. Anticipated Adverse Events

Anticipated adverse events are medical complications that are known to be associated with treatment of aortic aneurysms involving the renal-mesenteric arteries using GORE® [redacted] as a Bridging Stent with Branched and Fenestrated Endografts. See section 8, Risk Assessment.

9.1.1. Adverse Event Relationship

Each reported AE will be assessed by the investigator for its primary suspected relationship to the device, procedure, disease.

Only one primary relationship will be assigned to each reported AE.

[redacted]-related
The functioning or characteristics of the registry device caused or contributed to the adverse event.

Procedure-related
The procedure (and not the device) caused or significantly contributed to the adverse event (e.g., contrast induced renal failure, access vessel complication, etc.)*

[redacted]Procedure-related
The procedure (and not the device) to implant [redacted] caused or significantly contributed to the adverse event.

Device related ([redacted]and Gore accessory)
The functioning or characteristics of the device, other than [redacted] and Gore accessory, caused or contributed to the adverse event.

Disease-related
The adverse event was a result of the underlying disease progression for which the registry procedure is being performed, and not the device or procedure.

Gore Accessory related
The functioning or characteristics of the Gore accessory caused or contributed to the adverse event.

Not-related
An adverse event which cannot be attributed to the device, procedure, or disease.

Unknown relationship
The relationship of the adverse event to the device, procedure, or disease insert other categories as appropriate cannot be determined.

*Events related to the specific part of the procedure where [redacted] is implanted are not included in this definition

9.1.2. Adverse Event Classification

Each AE, regardless of the causal relationship with the device, will be assessed by the Investigator to determine if it is Serious or Non-serious, as defined below. The CEC will review this information and provide a final adjudicated classification.

Clinical Affairs uses the ISO 14155 definition for classification of severity.

Serious Adverse Event

A serious adverse event is an adverse event that led to any of the following:

(a) death

(b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:

(i) life-threatening illness or injury, or

(ii) permanent impairment of a body structure or a body function including chronic diseases, or

(iii) in-patient or prolonged hospitalization, or

(iv) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function

(c) fetal distress, fetal death, or a congenital abnormality, or birth defect including physical or mental impairment

NOTE: Emergency room visits and 23-hour observations may not constitute hospitalization.

Serious Health Threat

Signals from adverse events or device deficiencies are required to be evaluated by the Principal Investigator and reported to Gore immediately

9.1.3. Adverse Event Reporting and Coding

Adverse event reporting begins after enrolment, starting from index procedure date, and ends when the subject completes the 5 years visit. After enrollment all adverse events from the retrospective phase will be reported by the site in the EDC with the initial data entry. Adverse events that occur in the prospective phase will be reported as soon as possible.

For any condition reported in the medical history and / or present at baseline or index procedure do not report as an adverse event unless it becomes serious or increase in intensity, or if a worsening of a baseline condition is reported.

AEs will be reported on the appropriate CRF and documented in the subject's permanent medical record. The investigator at each site is ultimately responsible for reporting AEs to the sponsor.

The following information on each reported AE will be collected:

- Adverse event name
- Adverse event onset date
- Relationship
- Classification serious or non-serious
- Treatment

- Outcome
- Resolution date

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

Adverse event submission guidelines:

- Adverse event reporting begins once the patient is enrolled in the registry. All adverse events should be reported from enrollment through registry completion / discontinuation.
- Provide a diagnosis if possible. If unable to provide a diagnosis, report the symptoms as separate events. Adverse events should be reported using the full name without abbreviations or narratives.
- Adverse events with an outcome status of "ongoing" should be assessed at each follow-up evaluation to determine if the event has resolved. Adverse events ongoing at registry completion / discontinuation should be left as "ongoing" on the AE case report form.

9.1.4. Subject Death

In this registry, death is not considered an AE, but rather the outcome of an AE. An ongoing AE at the time of death or registry withdrawal will remain categorized as ongoing.

Attempts will be made by the Site to obtain death certificate and autopsy reports, when possible.

9.2. Unanticipated Serious Adverse Device Effects (USADE)

The sponsor is required to notify the appropriate regulatory agencies per local requirements of any USADE. Therefore, if a complication occurs that the investigator believes may be a potential USADE, the site should immediately contact the sponsor and EC to determine reporting requirements.

9.3. Device Deficiency

Device deficiencies are defined as Any inadequacy in the identity, quality, durability, reliability, safety, or performance of an investigational device, including malfunction, use errors, or inadequacy in information supplied by the manufacturer. All device deficiencies – even those that could have led to a SAE should be reported to the Sponsor immediately.

The following information on each reported deficiency will be collected:

- Description of deficiency
- Date of occurrence
- Batch code and lot number of the affected device
- Related subject, user or other persons AE information (if applicable)

Due to the retrospective approach, any device deficiency may have already been reported as part of the hospital's routine via Product Surveillance Group procedures. To close any potential gaps, sites are asked to report all device deficiency in the EDC.

9.4. Clinical Event Committee

An independent Clinical Events Committee (CEC) will review endpoint related clinical events during the registry to ensure the consistency of endpoints reported by the site. The [redacted] 21-04 CEC will be comprised of an interdisciplinary team of three members with pertinent expertise who are not directly involved in the conduct of the registry.

CEC will be managed by [redacted] to ensure the independency of the members from the sponsor.

Sponsor will not take part of any CEC activities and may only deliver initial training to the CEC members on the protocol and registry device.

After review, the CEC will inform [redacted] whether or not additional data is required to evaluate any specific event, whether or not clarifications are needed.

Site may need to send anonymized source documentation to CRO related to the events that need to be adjudicated by CEC.

This committee will operate under pre-specified procedures as outlined in its charter. The frequency of data review and other roles and responsibilities of the committee will be specified in the registry specific CEC charter.

10. Statistical Analysis

10.1. Registry Hypotheses

The registry is designed to statistically test the hypothesis that the Target Vessel Patency at 12 months (Primary Performance Endpoint) in both FEVAR and BEVAR populations of subjects is greater than 77%. The hypothesis will be tested separately in the two cohorts (FEVAR and BEVAR), using the subjects with imaging results available for the 12 months visit. The binomial exact test will be used with a one-sided 2.5% level of significance to test the null hypothesis.

The statistical hypothesis is specified as follows:

H_0: $P < 77\%$

H_A: $P \geq 77\%$

Alpha= 0.025 (one-sided)

Whereas P is the probability of maintaining Target Vessel Patency at 12 months.

The ITT population will be used to perform this test.

A separate analysis in the subgroup with mixed placement of branched and fenestrated endografts as well as other clinical uses not described as only FEVAR or BEVAR will also be assessed with no formal hypothesis.

10.2. Sample Size Assumptions

The assumptions used for the calculation of sample size in the registry included the anticipated performance of the [redacted] for the FEVAR and BEVAR procedures, the acceptance criteria determined from the l[redacted] The preliminary clinical evaluation suggested that the [redacted] in the FEVAR and BEVAR cohorts respectively.

10.3. Sample Size Determination

Using the above assumptions, the [redacted] enrolled in the FEVAR and BEVAR cohorts respectively.

10.4. Data Analysis

10.4.1. Timing of Analyses

The analysis to test the primary hypothesis will be conducted once all subjects have completed their 12 Month follow-up, data has been entered and cleaned in the EDC system. Subjects with a visit within 90 days of the annual time frames will be considered for analysis of the annual outcomes. [redacted]. The subject follow-up will continue for five years, and the final analysis will be done once all subjects have completed five-year follow-up. Separate analysis will be performed for FEVAR and BEVAR cohorts. No interim analysis for the early termination of registry is planned due to the post marketing usage of the [redacted] and retrospective nature of the enrollment. In addition, once the primary analysis has been performed and hypothesis tested, further analyses may also be performed as needed for annual reports, presentations and publications based on interim data or at any other time at the discretion of Gore.

10.4.2. Analysis Populations

Intent-to-Treat (ITT) dataset will consist of all enrolled patients meeting the inclusion / exclusion criteria and treated at least one vessel with the [redacted] ITT dataset will be used for the analysis of the primary and secondary endpoints. In addition, Per-Protocol dataset will also be created after excluding subjects not meeting inclusion/exclusion criteria or the vessels treated with the devices other than the [redacted]. Similarly, per vessel analysis will be performed with both datasets after identifying each vessel treated. Per vessel analysis will be further identified by type of main body portal and vessel treated e.g., BEVAR SMA, BEVAR Celiac, Fenestrated renal, BEVAR renal etc. and may include vessels from the cohort of subjects treated with mixed FEVAR/BEVAR procedures.

10.4.3. Registry Deviations

The registry protocol deviations will be assessed descriptively and their potential impact on the registry results will be evaluated considering the nature of such deviations. The sample size for the registry is increased by 10% to compensate for the missed visits to that extent and allow for the testing of the registry hypothesis without compromising the power.

10.4.4. Pooling of Data

All sites in the registry will follow a common protocol and the data will be monitored to assure compliance. The data collection and handling procedures will be the same at all registry Sites. As such, there is no concern in pooling data from different sites together for analysis. Gore may perform analyses to explore differences in device performance by gender, age, or any other subgroup of interest.

10.4.5. Statistical Analysis of Primary Endpoint(s)

Analysis of the Primary Endpoint to test the hypothesis will be performed using [redacted]. Missing data at the time of analysis will not be imputed.

10.4.6. Statistical Analysis of Secondary Endpoint(s)

Tables of each secondary endpoint will be [redacted] Missing data at the time of analysis will not be imputed.

11. Ethical and Regulatory Considerations

11.1. Statement of Compliance

The requirements of Clinical Investigation of Medical Devices for Human Subjects Good Clinical Practice (ISO14155-2020), International Conference on Harmonization Good Clinical Practice (ICH E6 (R2), have been incorporated into applicable Clinical Quality System procedures.

The following are applicable to this registry:

ICH-GCP E6 (R2)	International Conference on Harmonization Regulations Guideline For Good Clinical Practice
Regulation (EU) 2017/745	Regulation (EU) 2017/745 of the European Parliament and of the Council on medical devices,
ISO 14155:2020(E)	Clinical investigation of medical devices for human subjects – Good clinical practice

11.2. Compliance Responsibilities

The sponsor will conduct the registry in accordance with all applicable regulations and laws. The sponsor will be responsible for documenting that investigators have the necessary skills, training, and information to properly conduct the registry. The sponsor will confirm proper monitoring of the registry and verify that the site has obtained EC approval prior to enrollment. The sponsor will provide information to the investigators, the reviewing EC concerning the progress of and any new material information about the registry.

The investigator will conduct the registry in accordance with all applicable regulations and laws, any relevant agreements, the registry protocol, and all approval conditions of the reviewing EC. Any additional requirements imposed by the EC shall be followed. The investigator will verify EC approval is obtained prior to enrollment, maintained throughout the course of the registry, and that all EC reporting requirements are met. The investigator is responsible for protecting the rights, safety, and welfare of subjects under the investigator's care. The investigator is also responsible for ensuring that informed consent is properly obtained or a possible waiver documented as required.

The investigator will determine the cause and implement appropriate corrective and preventive actions to address significant noncompliance.

The registry shall be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

11.3. Informed Consent

The investigator shall verify that all potential subjects still alive and reachable for this registry are provided with an EC approved consent form describing this registry and sufficient information to make an informed decision about their participation. In case of deceased patients, the next of kin/legal representative could sign the informed consent form unless a waiver has been granted by the EC.

The formal consent of a subject, using the EC-approved consent form, must be obtained by the investigator or designee before that subject undergoes any registry-related follow-up procedure. The consent form will be signed and personally dated by the subject and the person who conducted the informed consent discussion. Next of kin/legal representative can sign on behalf of the subject if he/she is unable to make the decision to participate or if subject deceased at registry entry, (unless a waiver was granted), according to local regulations.

[redacted]

The original signed informed consent form will be retained in the subject records. A copy of the informed consent document will be given to the subject for his or her records. Any significant, new information which emerges while the registry is in progress that may influence a subject's willingness to continue to take part in the registry will be provided to the subject or LAR.

The investigator or designee shall verify that documentation of the acquisition of informed consent is recorded in each subject's records in accordance with applicable regulations.

Emergency contact details for reporting serious adverse events and serious adverse device effects will be listed in the EC-approved Informed Consent Form.

11.4. Regulatory Review

The investigator/ sub-investigator shall not enroll any subjects prior to obtaining approval from all required local authorities, including competent authorities and radiation committee.

In addition, the investigator/ sub-investigator shall not enroll any subjects prior to obtaining approval for the registry from a properly constituted independent EC.

The investigator will submit the protocol, informed consent forms, other information to be provided to subjects such as survey instruments or questionnaires, and any proposed advertising / recruitment materials, to the EC for written approval.

11.5. Conflict of Interest

All investigators/ sub-investigators will follow applicable laws and regulations as well as the conflict-of-interest policies of their site and the reviewing EC.

11.6. Confidentiality

All subject records will be kept confidential to the extent provided by applicable laws and regulations. The monitors and other authorized representatives of the sponsor may inspect all documents and records required to be maintained by the investigator, including but not limited to medical records.

Such records may also be reviewed by the site's EC and other regulatory bodies.

The investigator or designee will inform the subjects that their records will be reviewed.

11.7. Registry Discontinuation or Suspension

The entire registry may be suspended or prematurely terminated by the sponsor in the following cases:

- Serious adverse events as defined in section 9.1.2 attributable to the investigation.
- If new data become available which raises concern about the safety of the registry device, so that continuation of the registry might cause unacceptable risks to the subjects.
- If suspicion of an unacceptable risk to subjects arises during the registry, the sponsor may suspend the registry while the risk is assessed. The sponsor will terminate the registry if an unacceptable risk is confirmed.
- National regulatory authority withdrawal of registry approval.
- On recommendation by the CEC for any perceived safety concern based on clinical judgment, including, but not limited to, a higher than anticipated rate for any component of the safety endpoint, device failures resulting in AEs or unexpected SAEs.
- Administrative decision by the sponsor.

Registry participation of an individual registry site or an individual member of a registry site may be suspended or prematurely terminated by the sponsor in the following cases:

- If a principal investigator, EC or regulatory authority responsible for the registry has withdrawn approval for any reason.
- If sponsor monitoring or auditing identifies serious or repeated deviations on the part of the registry site or an individual registry investigator.
- If a site does not enroll any subjects.

Procedures for suspension or premature termination of this registry are:

- If the sponsor, EC or regulatory authority suspends or prematurely terminates the registry, all implanted subjects shall continue to be followed and treated as per standard of care at each site. The sponsor may request that subjects are contacted or complete an office visit prior to registry termination.
- The investigator of each site or authorized designee shall promptly inform the enrolled subjects.

- If the sponsor received notice that the EC and/or regulatory authority approval has been withdrawn for any reason, the sponsor shall notify the investigator as soon as possible and preferably within 24 hours. Enrollment must immediately cease until such approval is reinstated.
- If the investigator receives notice that the EC and/or regulatory authority approval has been withdrawn for any reason, the investigator shall notify the sponsor as soon as possible and preferable within 24 hours. Enrollment must immediately cease until such approval is reinstated.
- If the sponsor suspends or prematurely discontinues the registry the sponsor shall inform the investigators, the EC s and the authority of the rationale and provide them with the relevant data supporting this decision.
- If the registry (or a registry site) is prematurely terminated a routine close out visit as described in section 6.4 will be performed.
- If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator / institution should promptly inform the sponsor and the EC and should provide the sponsor and the EC a detailed written explanation of the termination or suspension.

The procedures of premature registry termination of an individual subject (voluntary withdrawal or withdrawal of the subject by the investigator) are detailed in section 5.2 of the registry protocol.

Procedure for resuming the registry after temporary suspension

- When the sponsor concludes an analysis of the reason(s) for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the sponsor shall obtain concurrence from the ECs and, where appropriate, the regulatory authority by providing the rational and relevant data supporting this decision before the registry resumes.
- When concurrence from ECs and, where appropriate, other regulatory authorities is obtained, the sponsor shall inform the investigators to resume the registry.
- If subjects have been informed of the suspension, the principal investigator or authorized designee shall inform them of the reasons for resumption.

12. References

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Registry-Specific Appendices

Appendix A: Eligibility Criteria with Justification / Rationale

Item Number	Text of Criterion	Rationale
I1	Patients treated with the [redacted] as a Bridging Stent in conjunction with a branched/fenestrated main body stent graft to allow endovascular aneurysm repair from 31 December 2021 until the 01 January 2017	[redacted]
I2	Age ≥18 years at the time of implant	[redacted]
I3	Provision of informed consent by the patient or next of kin/legal representative (for deceased patients at registry entry, unless a waiver was granted), according to local regulations.	[redacted]
[redacted]		
E1	Patients treated for ruptured aneurysm or who were otherwise hemodynamically unstable at the time of the procedure	[redacted]
E2	Patient treated for dissection acute or sub-acute, <90 days from presenting symptoms	[redacted]
E3	Patient treated using physician-modified endovascular grafts	[redacted] estrated and branched
E4	Patient intended to be treated with chimney, periscope octopus, sandwich technique per the pre treatment case plan.	[redacted]
E5	At the time of treatment, patient had known coagulation disorders including hypercoagulability that were not amenable to treatment	[redacted]
E6	Patient was pregnant at the time of treatment.	[redacted]
E7	Participation in another drug or device investigational drug or device study within one year of device implant, that can confound the registry endpoints.	[redacted]
E8	Patient had known or suspected systemic infection (including treatment for mycotic aneurysm) at the time of implant.	[redacted]

Appendix B: Zones of Attachment

For reporting purposes, the location and extent of stent-graft coverage will utilize a system of numerically labeled zones according to Figure 4.

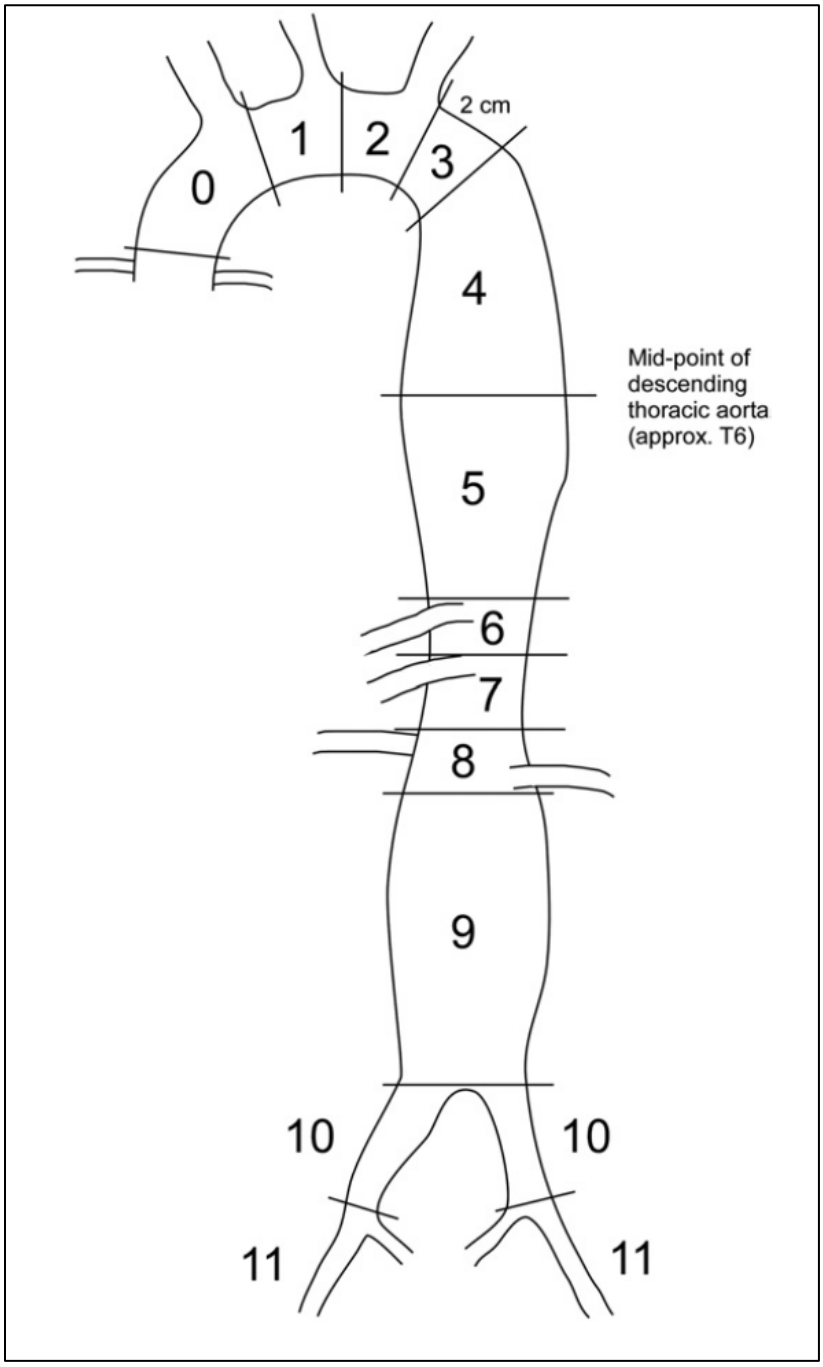

Figure 4 Zones of Attachment

Protocol Modification Summary

List of Changes in VBX 21-04 protocol version #2

The following administrative changes have been made to the protocol:

- Minor typographical and punctuation errors have been corrected throughout the protocol.
- In addition, the following changes have been made to the protocol:

Section	Changes to Protocol	Rationale	Potential impact on performance, effectiveness, safety or other endpoints
Inclusion/Exclusion criteria	Changed the wording of Inclusion criteria #1 to: *Patients treated with the* [redacted] *as a Bridging Stent in conjunction with a branched/fenestrated stent-graft to facilitate endovascular aneurysm repair from* [redacted]	Updated to extend screening and enrollment windows	[redacted]
	Changed the worlding of Exclusion criteria #4 to: *Patient intended to be treated with chimney, periscope, octopus, sandwich technique per the pre treatment case plan.*	Clarification of intent	This addition only provides clarification and will not affect study endpoints
Section 4.1 – description of the population	Maximum cap per site increased from 20 to 30 percent	Ward enrollment progression and meet powered simple size requirements	No impact
Section 5.5 – Pre-Screening	Added information about how phase one and	Adding details to clarify screening and	No impact

	phase two of the screening will occur	enrollment timeframe extension	
Section 10.4.1 – Timing of the analysis	Added information on visit windows that will be considered for analysis	Providing clarification	No impact