BSET-CLEVAR Registry

The British Society of Endovascular Therapy -ConformabLe EndoVascular Aneurysm Repair Registry:

A prospective, multi-centre, observational cohort study

Version number 3.1, 11/11/2021

MAIN SPONSOR: Imperial College London
FUNDER: The British Society of Endovascular Therapy (BSET) has received funds from W.L. Gore & Associates, Inc.
STUDY COORDINATION CENTRE: Imperial College London

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Protocol authorised by:

Name & Role	**Date**
Mr Colin Bicknell, B.M., M.D., F.R.C.S. Clinical Reader and Consultant Vascular Surgeon Chief Investigator	11.11.2021

Revision History

Protocol Version	Date	Amendments
1.0	28.03.2019	N/A – Original Protocol
2.0	09.05.2019	Removed the inclusion criteria statement that the informed consent form may be signed by a "legal representative".
3.0	09.12.2020	1. Timing of obtaining consent modified to allow consenting of participants *after* they undergo EVAR (within 30 days of procedure), if it was not possible to obtain consent pre-operatively. 2. The location of the Core Lab corrected from Liverpool University to Liverpool University Hospitals NHS Foundation Trust. 3. Study timeline revised and extended (due to pandemic delays)
3.1	11.11.2021	The maximum number of patients recruited per site revised from 20 patients to 30 patients. Competitive recruitment remains in place (*Non-substantial amendment, no study-wide review required*)

Study Management Group

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Clinical Queries

Clinical queries should be directed to either the Local Principal Investigator or the Study Coordinator who will direct the query to the appropriate person.

Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

Joint Research Compliance Office
Imperial College London and Imperial College Healthcare NHS Trust
Room 215, Level 2, Medical School Building, Norfolk Place
London, W2 1PG
Tel: 0207 594 9459/ 0207 594 1862
http://www3.imperial.ac.uk/clinicalresearchgovernanceoffice

Funder

The British Society of Endovascular Therapy (BSET) has received funds from W.L. Gore & Associates, Inc. to carry out this prospective, investigator-initiated study. BSET and the Sponsor (Imperial College London) will have full responsibility for the conduct of the study.

This protocol describes the BSET-CLEVAR study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the UK Policy Frame Work for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

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Glossary of Abbreviations

AAA	Abdominal aortic aneurysm
AE	Adverse Event
APTT	Activated partial thromboplastin time
BSET	The British Society of Endovascular Therapy
CDMS	Clinical Data Management System
CI	Chief Investigator
CRF	Case Report Form
CT	Computed Tomography
EPTFE	Expanded polytetrafluoroethylene
EVAR	Endovascular aortic aneurysm repair
EXCC device	GORE® EXCLUDER® Conformable AAA Endoprosthesis with ACTIVE CONTROL System
FEP	Fluorinated ethylene propylene
ICF	Informed Consent Form
IEP	Image Exchange Portal
IFU	Instruction for use
L-PI	Local Principal Investigators
PIS	Patient Information sheet
NHS	National Health Service
REC	Research Ethics Committee
SAE	Serious Adverse Event
SCC	Study Coordination Centre
UTI	Urinary tract infection

KEYWORDS

Abdominal aortic aneurysm; Endovascular aneurysm repair

Protocol version 3.1, dated: 11/11/2021
Favourable opinion given by South East Scotland Research Ethics Committee 01 on 12/01/2021

Study Summary

DESIGN A prospective, multicenter, observational cohort study of patients treated with the GORE EXCLUDER Conformable AAA Endoprosthesis **with ACTIVE CONTROL System** (EXCC Device)

AIMS The primary objective is to collect real-world clinical data and device specific outcomes of EXCC device in routine clinical treatment of abdominal aortic aneurysm (AAA).

OUTCOME MEASURES

Primary endpoint

Evaluation of positioning accuracy and aortic neck coverage expressed as percentage of the total aortic neck assessed by CT scan between 4 weeks and 3 months follow-up*

Secondary endpoints

- Technical success, defined as successful access and deployment of all required EXCC Device components
- In-hospital mortality
- Adjuncts to deal with type 1 endoleak at primary procedure
- Freedom from Type 1 or 3 endoleak at end of procedure, by 3* months and around 1* year
- 1-year aneurysm-related re-intervention rates
- 1-year aneurysm-related mortality

POPULATION Up to 200 patients presenting with abdominal aortic aneurysm (AAA) to the study centres (up to 30 NHS hospitals affiliated to BSET in the United Kingdom)

ELIGIBILITY Patients with AAA who are suitable for endovascular repair of their AAA and are either being considered for or have received treatment by endoprosthesis implantation

DURATION Approximately 38 months, including 12-month follow-up

* Timelines for the first and final follow-up are flexible: First follow-up, including CT scan imaging, may be carried out between 4 weeks and 3 months and second (final) follow-up, including either a CT scan or duplex U/S imaging (depending on local EVAR surveillance policy), may be done at 12 months ± 4 weeks.

1. INTRODUCTION

1.1 BACKGROUND

Disease

Abdominal aortic aneurysm (AAA) is a degenerative disease of the aorta. It has been estimated that the overall prevalence of AAA in the European population is 4-5%, and is associated with increasing age, male sex, a history of smoking, high blood pressure and hypercholesterolaemia. A family history of aneurysmal disease also contributes to the risk of AAA, as do the presence of peripheral vascular disease, chronic obstructive pulmonary disease and coronary artery disease[1].

Rupture of an AAA is responsible for approximately 1-2% of all male deaths over the age of 65 years. The AAA prevalence is approximately three times higher in men than in women[2], although the rupture rate is approximately three times higher in women than it is for men[3].

Historical Treatments

Endovascular aneurysm repair (EVAR) is a minimally invasive procedure designed to exclude an aneurysmal segment of the aorta from blood circulation, and is a well-established treatment for AAA. This minimally invasive approach to open surgical repair has led to a significant reduction in morbidity and mortality in the short term[4-6]. However, the durability of EVAR remains a concern, with late failure leading to rupture, and it is hoped that device evolution may lead to improved outcomes[7-9]. The EVAR procedure involves delivery of a stent graft compressed onto a catheter to an aneurysmal segment of the aorta from a remote access site, generally the femoral artery. EVAR was first described in 1991 by Juan Parodi[10]. Since that time, EVAR for the treatment of AAA has shown a lower operative and aneurysm related mortality in numerous clinical trials when compared with open surgical repair[11]. These results have led to the widespread adoption of the EVAR procedure in patients with infrarenal AAA.

All endovascular devices are designed and tested for use in defined range of anatomies, described in the respective Instructions For Use (IFU) for each device. However, these anatomical criteria describe a subset of all patients that present with AAA and so use in patients outside of the IFU is common in order to treat to broadest range of patients. To facilitate this, interventionists have developed a range of off-label endovascular techniques which can extend the potential pool of patients eligible for endovascular treatment. However, use of the devices outside of IFU indications and with adjunctive

techniques such as chimney grafts can compromise the durability of the repair and may be associated with a higher risk of complications. Patients treated with 'hostile' neck anatomy, often with more severe neck angulation or shorter effective proximal sealing zones are at increased risk for operative morbidity, additional adjunctive procedures at treatment, Type I endoleak at one year, and aneurysm related mortality at one year[12].

The continued off-label use of endovascular stent grafts to treat patient populations with challenging anatomy suggests a need for improved endovascular stent grafts so that these patients can be treated safely and effectively in line with the manufacturer's intentions, the graft design and testing, and the indications provided in the Instructions For Use.

1.2 RATIONALE FOR CURRENT STUDY

Study Device Description

The GORE EXCLUDER AAA Endoprosthesis is a stent graft device that has accrued 20 years of worldwide experience with more than 285,000 devices implanted. Extensive clinical and commercial data has proven it to be a safe, effective and durable treatment for AAA.

The GORE® EXCLUDER® Conformable AAA Endoprosthesis *with ACTIVE CONTROL System* (EXCC Device), which is CE Mark approved, is an evolution of this device with a modified trunk design that enhances its ability to conform to the specific patient aortic neck anatomy. This has the potential to allow more accurate deployment, greater neck coverage and sealing zone especially in more angulated anatomy and improved durability of treatment.

The EXCC Device provides endovascular treatment of infrarenal AAA. It is a self-expanding stent graft that is constrained onto a delivery catheter which is used to advance and deploy the stent graft at the target location. The EXCC Device is a multi-component system consisting of a Trunk-Ipsilateral Leg Endoprosthesis, a Contralateral Leg Endoprosthesis, an Aortic Extender Endoprosthesis for proximal extension, and an Iliac Extender Endoprosthesis for distal extension. The graft material consists of expanded polytetrafluoroethylene (ePTFE) and fluorinated ethylene propylene (FEP) that is supported by nitinol (nickel titanium alloy) wire along its external surface. Nitinol anchors and an ePTFE / FEP sealing cuff are located at the leading (proximal) end of the trunk and a sealing cuff is located at the leading (proximal) end of the Aortic Extender. All components have gold radiopaque markers for visualization. ePTFE / FEP sleeves are used to constrain the endoprostheses on the delivery catheter.

Controlled deployment of the device is enabled with a staged deployment system including optional angulation control.

2. STUDY OBJECTIVES

Primary Objective(s)

The primary objective is to collect device-specific performance outcomes of GORE EXCLUDER Conformable AAA Endoprosthesis with ACTIVE CONTROL System in routine clinical treatment of abdominal aortic aneurysm.

Secondary Objective(s)

The secondary objective(s) are assessment of technical and clinical success, as well as the evaluation of real-world clinical outcomes of GORE EXCLUDER Conformable AAA Endoprosthesis with ACTIVE CONTROL System in routine clinical treatment of abdominal aortic aneurysm.

3. STUDY DESIGN

3.1 DESCRIPTION OF STUDY DESIGN

The study is a prospective multicenter observational cohort registry of patients treated with the GORE® EXCLUDER® Conformable AAA Endoprosthesis with ACTIVE CONTROL System in the UK. Recruitment will take place in up to 30 experienced UK centers with extensive EVAR experience and implanted five or more GORE endoprosthesis. Up to 200 patients will be recruited and followed up for 1-year. It is anticipated recruitment will be complete in ~2 years and that the study will run for ~ 3 years. The maximum number of subjects enrolled per site is 30. All screened patients will have been previously evaluated in a standard manner (as part of their routine care) for their anatomical suitability for EVAR with CT (see section 4.1 for further details on patient identification and screening assessment). All patients will undergo post-operative CT between 4 weeks and 3-months post implantation in line with routine local surveillance policies following EVAR and further follow-up to 1-year will be at the discretion of the implanting center.
Patients may be enrolled into the study provided all inclusion and no exclusion criteria are met as specified in Section 4. Procedural details may vary between sites, but all will follow standard hospital

protocol for EVAR and patient care management. Subjects will be evaluated through hospital discharge and return for follow-up visits between 4 weeks and 3 months and at 12 months ± 4 weeks.

3.2 STUDY OUTCOME MEASURES

Primary Endpoint

Evaluation of positioning accuracy and aortic neck coverage expressed as percentage of the total aortic neck assessed by a follow-up CT scan between 4 weeks and 3 months.

Endograft neck utilization will be assessed by Core lab analysis. The surface area of infra-renal neck will be calculated by assessment of the preoperative CT scan. Post-operative CT will be performed between 4 weeks and 3-months and the surface area of aortic neck covered by the GORE® EXCLUDER® Conformable AAA Endoprosthesis with ACTIVE CONTROL System will be calculated as a percentage of the pre-operative surface area.

Secondary Endpoints

- Technical success defined as successful access and deployment of all required EXCC Device components
- In hospital mortality
- Adjuncts to deal with type 1 endoleak at surgery
- Freedom from Type 1 or 3 endoleak at end of procedure, 3 months and 1 year
- One-year aneurysm-related re-intervention rates
- One-year aneurysm-related mortality

4. PARTICIPANT ENTRY

4.1 IDENTIFICATION AND SCREENING

The target patient population for the GORE® EXCLUDER® Conformable AAA Endoprosthesis with ACTIVE CONTROL System registry is a consecutive series of patients who undergo endovascular

treatment for abdominal aortic aneurysm. Prior to study-specific screening, all patients will have had a CT scan as part of their routine care and they will have been identified for routine treatment of their AAA by EVAR after meeting accepted surgical threshold criteria. These patients will then be screened for potential inclusion in the BSET-CLEVAR registry by review of their medical notes by vascular clinicians from the patient's existing clinical care team at the participating hospital or during the vascular multidisciplinary team (MDT) meeting, or in person during a routine appointment at the Vascular Out-patients clinic. If deemed suitable, the patient will be provided with study-specific patient information sheet (PIS) by their Vascular Surgeon or Vascular Specialist Nurse, either in person during a routine appointment (in which case they will be given a minimum of 24 hours to consider participating in the registry), or by post prior to their routine appointment/hospital visit. If the latter, the PIS will be sent to the potential Participant in pre-paid envelopes (provided by the study co-ordinating centre) before the patient's routine vascular out-patients appointment or hospital admission, so that the patient will have had time to read the information before they visit the hospital. They will have opportunity to discuss the information contained in the PIS with their Vascular Surgeon/Vascular Specialist nurse and asked to consider participating in the registry.

Written consent will be obtained from those patients who agree to participate either before *or* after their operation and they will be assigned a study ID number. If written consent is being obtained after EVAR, this will be done within 30 days of implantation. Only patients who meet all of the inclusion criteria and none of the exclusion criteria specified below will be enrolled. At each participating hospital, a log of all screened patients will be kept locally, which will record basic demographic data (patient initials/year of birth/sex; to ensure patients have not been recorded in duplicate) and reasons for non-eligibility.

4.2 INCLUSION CRITERIA

Indication for aortic endovascular stent graft repair as determined by the treating physician.
The patient is / has:

- Age 55 or more at the time of informed consent signature.
- Non-ruptured infra-renal AAA that requires treatment, and in the opinion of the Investigator, whose anatomy is adequate to receive or has already received the GORE® EXCLUDER® Conformable AAA Endoprosthesis **with ACTIVE CONTROL System** (EXCC device).

- An Informed Consent Form dated and signed by the Subject either before *or* within 30 days of EXCC device implantation

4.3 EXCLUSION CRITERIA

The patient is / has:

- Previous infra-renal aortic surgery prior to the implantation of the EXCC device
- Been treated in another aortic or thoracic medical device study within 1 year of study enrollment.
- Active infection
- Penetrating aortic ulcer or dissection or intramural haematoma in the treated segment
- Any clinically significant medical condition, which in the opinion of the investigator, may interfere with the study results or reduce life expectancy to <2 years
- In the opinion of the investigator unable or unwilling to comply with the requirements of the study.

4.4 WITHDRAWAL CRITERIA

A Participant may withdraw from observational data collection at any time and should notify the participating site in this event. It is important to encourage patients to return for both follow-up visits. The local PI may also withdraw the Participant from the study at any time based on his / her medical judgment.

5. ADVERSE EVENTS AND REPORTING PROCEDURES

5.1 RELATED AND ANTICIPATED ADVERSE EVENTS

Patients with AAA undergoing EVAR have the potential risks of treatment and complications that are known to be associated with endograft implantation. Competent, experienced medical/surgical staff will perform all procedures and every effort will be made to prevent adverse events. The adverse events listed below are anticipated procedure-related risks:

Anticipated risks that do **not** need expedited reporting		
Access vessel dissection or rupture	Graft migration	Respiratory failure
Amputation	Graft limb	Spinal cord ischaemia
Aortic rupture	thrombosis/stenosis/occlusion	Stroke
Buttock claudication	Haemorrhage	UTI
Chest infection	Limb ischaemia	Visceral ischaemia
Endoleak	Multiple organ failure	Wound infection
Graft infection	Myocardial infarction	
Graft kinking	Renal failure	

Risk-to-Benefit Rationale: As this is an **observational study of real-world routine clinical practice,** there are **no additional** benefits or **risks dependent upon participation** in the registry.

5.2 SERIOUS ADVERSE EVENTS

5.2.1 Serious Adverse Event ISO 14155 Definition

Serious Adverse Events (SAE) are defined as those adverse events that

- leads to death
- leads to serious deterioration in the health of the participant that either results in
- a life-threatening illness or injury, or
- a permanent impairment of a body structure or body function, or
- in-patient or prolonged hospitalization, or
- medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body structure or a body function

5.2.2 Serious Adverse Event (SAE) Relationship to device, procedure or disease

Each reported SAE will be assessed by the local Principal Investigator for its primary suspected relationship to the device, procedure, disease and patient co-morbidity, as per the definitions given below. Given this is an observational registry and the endograft implantation is part of patient's routine treatment for their AAA (i.e. **not** a research procedure), only **related** and **unexpected** SAEs (i.e. those not listed in section 5.1) will be reported on the SAE form.

Study Device-related
The functioning or characteristics of the device caused or contributed to the SAE.

Study Procedure-related
The procedure (and not the device) caused or significantly contributed to the SAE.

Disease-related
The SAE was a result of the underlying AAA progression for which the study procedure is being performed, and not the device or procedure.

Not-related
A SAE which cannot be attributed to the device, procedure, or AAA. These will *not* be captured.

5.2.3 SAE Reporting Procedures

- As above, only those SAEs that have been assessed as **related** (to the disease, device and/or implantation technique) **and** that are **unexpected** (i.e. those not listed in section 5.1) will be reported using the Serious Adverse Event Form, which will also be documented in the participant's permanent medical record.
- The following information on each reported Serious Adverse Event will be collected:
    - Description and, if possible, diagnosis*
    - Onset Date
    - Relationship

- Classification
- Severity
- Frequency
- Treatment
- Outcome
- Resolution Date

* If unable to provide a diagnosis, report the symptoms as separate events.

- The local Principal Investigator at each Site is ultimately responsible for reporting **related and unexpected SAEs** to the Chief Investigator, and must do so immediately or within 24 hours of being made aware of the event. Local PI should also report this to the endograft manufacturer through normal product surveillance mechanisms.

Chief Investigator contact details for reporting SAEs
Fax: 020 7886 2216, attention Mr Colin Bicknell
Please mark "URGENT"
Tel: 020 3312 6072 (Mon to Fri 09.00 – 17.00)

- **Death**, including cause of death, must always be reported on the SAE form.

- The initial report can be made verbally but must be promptly followed with a detailed, written report on the study SAE form provided in the BSET-CLEVAR CRF Booklet.

- The local PI should ensure that follow-up information is provided when available. Where supporting documents are sent with this form, these must be anonymised. Where the information available is incomplete at that time, as much information as can be ascertained should be sent to ensure timely reporting, with additional information provided as soon as it is known. Additional information received for an event (follow-up or corrections to the original event data) needs to be detailed on a new Serious Adverse Event Reporting Form.

- Reports of **related and unexpected SAEs** should be reported to the Sponsor and to the South East Scotland Research Ethics Committee 01 within 15 days of the Chief Investigator

becoming aware of the event using the NRES SAE form for non-IMP studies. The Chief Investigator must also notify all local PIs at participating centres.

- Serious Adverse Events with an outcome status of "Ongoing" should be assessed at each follow-up evaluation to determine if the event has resolved. Serious Adverse Events ongoing at study completion / discontinuation should be left as "Ongoing" on the SAE case report form.

6. ASSESSMENT AND FOLLOW-UP

6.1 SCHEDULE OF EVENTS

	Screening/ Baseline	Prior to procedure	Procedure	Discharge	1st follow-up (4 weeks to 3 months post-op)	2nd follow-up (12 months ± 4 weeks post-op)
Informed Consent (option to recruit *before* or *within 30 days* of procedure)	X	X		X	X (within 30 days only)	
Demographics and Medical History	X#	X#				
Physical Examination	X#	X#		X		
Blood results	X#	X#				
ASA risk classification & operative details			X			
SAE assessment (related and unexpected events only)				X	X	X
CT Scan+	X				X	X*
Duplex Ultrasound+						X*

*12 months follow-up imaging type (CT or duplex) will be at the discretion of the implanting site.

Demographics & Medical history information, physical examination and blood test results are all standard of care procedures prior to EVAR (i.e. no extra tests or procedures solely for the study) and they can either be obtained during screening assessment **or** at a subsequent routine appointment at the Vascular Out-Patients clinic prior to endograft implantation.

+Pre-op CT scan before EVAR and post-op CT and/or duplex ultrasound after EVAR are standard of care imaging investigations; BSET-CLEVAR Registry will only collect and evaluate these routine imaging data and the study does not involve any additional imaging investigations.

6.2 PRE-PROCEDURE EVALUATIONS

The following evaluations, which are *standard of care before undergoing EVAR*, must be completed **prior to** treatment of the patient by GORE® EXCLUDER® Conformable AAA Endoprosthesis with ACTIVE CONTROL System:

- Demographics
- Medical history
- Physical examination
- Chemistry
- Haematology
- APTT
- Serum Creatinine
- CT

6.3 PROCEDURE

The Sponsor and the funder will not impose requirements that limit health care professionals from exercising their best medical judgment for treatment. Therefore, patient selection, diagnostic imaging and treatment interventions will be determined by physicians based on clinical practice standards. No specifications for device use, indication, follow-up schedule or requisite data collection outside of the site's routine practice will be required.

Patients who meet the BSET-CLEVAR registry inclusion Criteria andare treated with the Gore Conformable AAA Endoprosthesis with ACTIVE CONTROL System at participating sites will be considered enrolled in the BSET-CLEVAR registry once they sign the study-specific informed consent form, either *before* or *within 30 days* of device implantation.

6.4 REPEAT INTERVENTIONS

Aneurysm-related re-interventions performed after the initial treatment and within the first year should be recorded in the separate re-interventions CRF.

6.5 FOLLOW-UP

Follow-up will be as prescribed by the participating institution and/or health care professionals. If a Participant does *not* return to the site for follow-up evaluation, it is requested that the site contact either the patient, patient's next of kin/representative or the patient's GP for survival determination.
A post-operative CT scan must be performed between 4 weeks and 3 months following primary procedure and the images transferred to the Core-Lab, as detailed in section 7.3.
Re-interventions and additional device deployment should be recorded on the Re-interventions CRF.

6.6 SUBJECT LOST TO FOLLOW-UP

A Participant will be considered lost to follow-up and withdrawn from the study once they have missed three consecutive follow-up appointments and/or imaging appointments and three documented attempts have been made by the Investigator or designee to contact the Participant or next of kin.

6.7 SUBJECT STUDY COMPLETION

A Participant will have completed the study 1-year after device implantation when all follow-up visits and imaging have been completed and recorded in the CRFs and copies of DICOM images sent to the Core Lab. Any Participant who does not complete these requirements due to voluntary withdrawal, physician withdrawal, death, or any other reason will be considered a withdrawal.

6.8 DEVICE DEFICIENCIES

Participating sites will adhere to their current commercial contractual agreement with the Device manufacturer for device shipping, storage, use and return. Implanted device part numbers will be collected on the "Devices Implanted" CRF. Device failures/complications should be recorded in the relevant CRF and, if deemed unexpected, also reported on the SAE form. They should also be reported through normal product surveillance mechanisms.

7. STUDY MANAGEMENT AND ADMINISTRATION

The day-to-day management of the study will be co-ordinated by the Study Manager based at the Study Coordination Centre at Imperial College London, reporting to the Chief Investigator. The Study Manager will liaise with local principal investigators (L-PI) to ensure that the study is conducted locally according to protocol and in an expeditious manner.

7.1 STUDY CO—ORDINATING CENTRE

The Study Co-ordinating Centre (SCC) is responsible for the overall coordination of the Study, including:

- Study planning and organization
- Agreement of each local recruitment plan
- Contractual issues with local study sites
- Preparation of HRA and Research Ethics Committee (REC) applications
- Liaison with regulatory authorities and other outside agencies to ensuring compliance with current legislation and research governance
- Conducting a set up/initiation visit to each site (if necessary, remotely, to avoid delays to site start-up) to explain study protocol and procedures to relevant staff, and provide study-specific training, where necessary
- Auditing and monitoring of overall progress of the study, which will include:
    - Visits to all sites to support data collection, facilitate CT image transfer and CRF completion.
    - After implantation of 3-5 grafts which are entered into the registry, the study co-ordinator will review the data recorded for any discrepancies, and if deemed necessary, will return to the sites and ensure accuracy of the study data collected by direct examination of the source data with the study team.
    - In addition, any sites where concerns are raised will be visited and 20% of records examined as above.
- Clinical safety monitoring (including working with the Chief Investigator to facilitate reporting of relevant SAEs to the Sponsor, and if applicable, to the REC)
- Responding to queries from local study sites

7.2 LOCAL STUDY SITES

The local principal investigators (L-PI) and clinical staff at the local study sites are responsible for:

- helping facilitate local management approval (aided by the Study Coordinating Centre)
- completing study training and adhering to regulatory requirements (GCP, use of study database etc)
- identification of potentially eligible patients
- conducting study procedures and follow-up according to study protocol and recording and reporting protocol deviations to the Chief Investigator
- prompt reporting of related and unexpected SAEs to the Chief Investigator (using the SAE form) and endograft manufacturer through normal product surveillance mechanisms
- facilitating the transfer of pre- and post-operative CT scans to the Core lab using the NHS image transfer system, Image Exchange Portal (IEP) (or failing that, using de-identified DICOM images saved on CDs as described in section 7.4)
- dealing with routine enquiries from patients and their families
- obtaining appropriate information to confirm potential primary and secondary study endpoints

7.3 Data Collection and Submission

The Clinical Data Management System (CDMS) for this study will be provided by Liverpool University Hospitals NHS Foundation Trust.

Data Collection Methods

Online submission of Case Report Forms (CRFs) will be performed in real time. The local team will be able to complete hard copies of CRFs, if desired, before recording the data in the CDMS (hard copies will be retained in the implanting centers).

Data Clarification and Correction

The Study Co-ordinator will monitor data collection and seek clarification and correction of discrepancies and missing data items.

Case Report Form Completion Schedule

All CRFs should be completed within 15 days of device implantation. A CRF Booklet is available as a separate document.

7.4 CORE LAB

Core Lab services for this study will be provided by Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK.

Pre and post-operative CT scans will be transferred to the Core lab by the NHS image transfer system, Image Exchange Portal (IEP). Core Lab will use the NHS number to retrieve your CT scans from the IEP. In case of problems with IEP transfer, DICOM images will be de-identified by removing patient identifiers (name/hospital number/dob) and replacing these with the patient's study ID, and de-identified images will be sent to the Core Lab on a CD) . CT evaluation will be performed by trained investigators on 3-D reconstructions of pre and post-operative images.

Following the end of the study, fully anonymised DICOM images may be made available to BSET and the endograft manufacturer for teaching and training purposes.

7.5 PROTOCOL DEVIATIONS

A Protocol deviation is defined as any change, divergence, or departure from the study design or protocol. The local PI is responsible for promptly recording and reporting protocol deviations to the Chief Investigator, who may, depending on the severity, cascade this information to the Sponsor and the reviewing Ethics committee per Ethics committee policy. The Sponsor will determine the effect of the protocol deviation on the scientific soundness of the study and Participant safety and determine if additional reports or actions are required. Additional action may include site re-training and / or Site termination.

The Chief Investigator will not implement any changes to the protocol without first obtaining written agreement from the Sponsor and documented approval from the Ethics committee, except in the event

of an immediate hazard(s) to a Participant. The Chief Investigator will report the Protocol Deviation in accordance with the applicable regulations.

7.6 PROTOCOL AMENDMENTS

The Chief Investigator will obtain Ethics committee approval on all amendments in a timely manner. The Study Co-ordinating Centre will confirm proper training of participating centre staff on all protocol amendments.

7.7 ACCESS TO SOURCE DATA/DOCUMENTS

Source data are defined as all information necessary for the reconstruction and evaluation of the Clinical Investigation. The local PIs will keep all study records, source data and investigational devices available for inspection by the Sponsor, Study coordinating Centre personnel, Ethics committee and regulatory authorities (also see section 7.1 for auditing & monitoring).

7.8 STUDY RECORDS RETENTION

Both the Chief Investigator (delegated to Study Coordinator) and the local PIs will maintain complete, accurate and current study records as required by applicable regulatory requirements. Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period. In any event, study records will not be disposed of, nor custody of the records transferred, without prior written approval from the Sponsor and the Funder.

8. STATISTICS AND DATA ANALYSIS

The aim of this prospective, observational study is to collect data on the performance of the device in terms of neck coverage and the sample size assumption is that it is an observational study and up to 200 patients is a reasonable achievable number of patients to gain enough data to make a useful assessment and also to provide sufficient data to plan a future comparative study.

8.1 Sample Size Assumptions

The current evidence related to stent graft utilization of the aortic neck surface area is limited. This study will provide data on which to base power calculations for future studies.

8.2 Sample Size Determination

As above, the sample size is up to 200 patient implants across up to 30 UK centres. Operative mortality is estimated to be 1% and 1-year survival estimated at 90-95%. It is estimated 180-190 patients will complete the study.

8.3 PLANNED ANALYSES

Timing of Analyses

Core lab CT analysis will be performed on pre- and post-operative CT images at study completion.

Analysis Populations

The entire 200 patient registry population

Statistical Analysis of Primary Endpoint(s)

The median aortic neck surface area utilized will be calculated from pre- and post-operative CT images. If post-operative CT images between 4 weeks and 3 months following primary procedure are not available, the Participant will be excluded from analysis.

Statistical Analysis of Secondary Endpoint(s)

Categorical variables will be expressed as percentages. Continuous variables are presented as mean ± standard deviation.

Determinants of poor neck apposition

Multivariate analysis will be conducted to determine which of the demographic, procedural, anatomical factors are related to poor neck apposition in the cohort.

No formal interim analyses are planned. Basic descriptive methods will be used to present the data on study participants, study conduct, clinical outcomes and safety. A detailed statistical analysis plan (SAP) will be written prior to the final analysis.

9. ETHICAL AND REGULATORY CONSIDERATIONS

9.1 ETHICS APPROVAL

The Study Coordination Centre has obtained approval from the South East Scotland Research Ethics Committee (REC) 01 and Health Regulator Authority (HRA). The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

9.2 CONSENT

Consent to enter the study must be sought from each Participant only after a full explanation has been given, an information leaflet offered and time allowed for consideration (minimum 24 hours). The formal consent of a Participant using the approved consent form, must be obtained by the local PI (or designated colleague detailed in the delegation log) before EVAR or within 30 days of EVAR and study data must not be collected until informed consent has been obtained. . The consent form will be signed and personally dated by the Participant or legally authorized representative, and the person who conducted the informed consent discussion. The original signed informed consent form will be retained in the Participant's hospital records. A copy of the informed consent document will be given to the Participant for his or her records, and an additional copy filed in the Participant's study file. Consent of vulnerable patients should be obtained in line with local hospital policy

The right of the Participant to refuse to participate without giving reasons must be respected. After the Participant has entered the study the clinician remains free to give alternative treatment to that specified in the protocol at any stage if he/she feels it is in the Participant's best interest, but the reasons for doing so should be recorded. In these cases the Participant remains in the study for the purposes of follow-up and data analysis. All Participants are free to withdraw at any time from the protocol treatment without giving reasons and without prejudicing further treatment. In addition, any significant, new information which emerges while the study is in progress that may influence a Participant's willingness to continue to take part in the study will be provided to the Participant.
The local PI shall verify that documentation of the acquisition of informed consent is recorded in each Participant's records in accordance with applicable regulations.

9.3 CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act. All participant records will be kept confidential to the extent provided by applicable laws and regulations. Each Participant will be assigned a study specific ID number and this study number will be used for all correspondence and data storage. The patient master list which will include the study ID, patient name, date of birth and NHS number and name of recruiting hospital will be treated in strictest confidence and will be stored on a dedicated, non-networked standalone computer with Microsoft BitLocker full disk encryption, only accessible to the Study Manager. The web-based database containing data collection forms will use pseudonymised data with patient's study ID only, and will never include patient names. Patient identifying data will not be used when publishing results. The study coordinating centre staff and other authorized representatives of the Sponsor may inspect all documents and records required to be maintained by the local PI, including but not limited to medical records. Such records may also be reviewed by the central and local ethics committees and R&D department.

9.4 INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

9.5 SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

9.6 FUNDING

The British Society of Endovascular Therapy (BSET) has received funds from W.L. Gore & Associates, Inc. to carry out this prospective, investigator-initiated study. BSET and the Sponsor (Imperial College London) will have full responsibility for the conduct of the study. Each participating centre will receive a reimbursement of £200 for each patient recruited into the registry for time taken for identifying patients, obtaining consent and collecting study data.

9.7 CONFLICT OF INTEREST

All Investigators will follow applicable laws and regulations as well as the conflict of interest policies of their Site and the reviewing Ethics Committee.

10. PUBLICATION POLICY

It is the intent of the Sponsor that the multicentre results of this study will be submitted for publication (in a peer reviewed journal). The Study Management Group (named on page ii) will review the multicenter results and write and submit publications at the completion of the study.

In addition, the findings will be disseminated to vascular surgeons and other health care professionals at research and educational meetings organised at local, regional, national and international levels. All analyses will be performed in compliance with a pre-defined analysis plan. The Chief Investigator and the study management team will be responsible for drafting the main reports from the study.

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