AAA-SHAPE Pivotal Trial: Abdominal Aortic Aneurysm Sac Healing and Prevention of Expansion

Published: 19-11-2024
Last updated: 31-01-2025

The purpose of the pivotal study is to determine the safety and efficacy of IMPEDE-FX RapidFill for increasing the percentage of subjects with shrinkage of the abdominal aortic aneurysm sac when used as an adjunct to on-label EVAR stent graft...

Ethical review	Approved WMO
Status	Pending
Health condition type	Aneurysms and artery dissections
Study type	Interventional

Summary

ID

NL-OMON57110

Source
ToetsingOnline

Brief title
AAA-SHAPE Pivotal Trial

Condition

- Aneurysms and artery dissections

Synonym
Bulge or swelling due to weaking of the walls of the aorta

Research involving
Human

Sponsors and support

Primary sponsor: Shape Memory Medical
Source(s) of monetary or material Support: Shape Memory Medical Inc.

Intervention

Keyword: Abdominal Aortic Aneurysm, Aortic Diseases, Cardiovascular Diseases, Vascular Diseases

Outcome measures

Primary outcome

Primary Effectiveness Endpoint:

The percentage of subjects showing regression, defined as sac volume reduction

of >=10% at 1 year, and no AAA-related intervention through 1 year.

Sac volume reduction is defined as the AAA volume (minus the stent graft

volume) at the 1-year visit minus the same measurement at the 30-day visit.

Dividing this difference by the volume measurement at the 30-day visit yields a

percentage reduction (volume shrinkage will be a negative number).

Primary Safety Endpoint:

Freedom from the following through 30 days post-index procedure:

• Major adverse events (MAEs)

o MAEs (CEC adjudicated) include the following: all-cause mortality, bowel

ischemia, myocardial infarction, paraplegia, renal failure, respiratory

failure, stroke, procedural blood loss >1000 mL. MAEs are further defined below.

• AAA-rupture or AAA-perforation

• Conversion to Open Repair

Secondary outcome

Key Secondary Effectiveness Endpoints:

• The percentage of subjects showing regression, defined as sac diameter

reduction of >=5mm at 1 year, and no AAA-related intervention through 1 year.

• Incidence of large endoleaks (>2.4) through 1 year

• Incidence of sac diameter enlargement through 1 year

• Incidence of Type II endoleak and sac diameter enlargement through 1 year

Secondary Effectiveness Metrics:

The following metrics are determined at the time of investigational device implant:

• Technical failure (defined as failure to implant at least 100% of the calculated minimum number of IMPEDE-FX RapidFill Implants into the AAA sac, or exceeding the maximum number of implants)

• An indication of the amount of sac filling: the number of IMPEDE-FX RapidFill Implants inserted.

The following metrics are determined at each follow-up visit:

• Change in both AAA sac diameter and volume at 6 months, 1 year, and annually, based on the diameter/volume determined from the 30-day CTA.

• Rate of endoleaks, overall and stratified by type

• Other EVAR measures of success/failure (impact of IMPEDE-FX RapidFill to be discussed)

o EVAR graft migration, patency, stenosis, kinking

The following metric is Adverse Event (AE) based and is recorded as AEs are observed by the site:

• Rate of secondary AAA-related interventions, as adjudicated by the CEC

Secondary Safety Metrics:

The following metrics are AE based and are recorded as they are observed by the site:

• All MAEs from the day of procedure through all time points. Relatedness to the investigational product/procedure to be adjudicated by the CEC.

• All serious adverse events (SAEs) through all time points. Relatedness to the investigational product/procedure to be adjudicated by the CEC.

• Rate of conversion to open AAA repair

• Rate of AAA-rupture or AAA-perforation

• Rate of access site complications

• Clinically significant misplacement or migration of the IMPEDE-FX RapidFill Implants or EVAR implant, defined as requiring surgical or endovascular intervention.

• Vessel injury caused by the IMPEDE-FX RapidFill or EVAR implantation procedure, requiring surgical or endovascular intervention.

The following metric can occur in and around the initial implantation procedure:

• Post-implantation Syndrome rate, measured through the 30-day follow-up.

o Fever (temperature > 38C) and white blood cell (WBC) count >12 thousand/µL in the absence of infection

Other Measurements:

• Procedural Information, e.g.,

o Stent graft used

o Duration of procedure

o Access Method

• Anticoagulation/antiplatelet/statin usage

• Serum C-Reactive Protein (CRP)

• Anatomical measurements from CT at baseline and follow-up time points.

• Quality of Life Survey

• Hospital care metrics (both the initial procedure and AAA-related secondary

interventions):

o Hospital length of stay

o Length of procedure

o Duration of ward stay

Study description

Background summary

An abdominal aortic aneurysm (AAA) is an enlarged area in the lower aorta. Over time, this enlargement (often called an aneurysm sac) can become weak, and the force of normal blood pressure can cause it to expand and rupture. This can lead to hemorrhage and death.

The prevalence of AAA is 4-8% worldwide and increases in people >60 years. The main risk factors for AAA are increased age, male gender, smoking, hypertension, atherosclerosis and a family history of AAA. As men are 4 times more likely to develop an AAA, it is recommended that men should be screened for AAA beginning at 65 years of age. AAAs are difficult to detect as they are largely asymptomatic unless they are rapidly expanding or ruptured. They are mostly detected during abdominal imaging for another indication.

Left untreated, an AAA is at risk of continued growth and rupture. AAA risk factors include smoking, high salt intake, high blood pressure, concomitant peripheral arterial disease and cerebrovascular disease, and family history of AAA. Elective repair is recommended for AAA >=5.5 cm in diameter in men and >=5.0 cm in women.

Left untreated, the aneurysm will continue to grow and will eventually rupture.

Ruptures are harder to treat, and 80% of ruptures result in death. Biomechanical stresses on the artery, such as greater flow lumen volume and lower thrombus burden (defined as the percentage of the AAA sac volume occupied by thrombus), increase the risk of rupture. Aneurysms with higher thrombus burden are less likely to grow. Therefore, thrombus burden is a factor that could be used for risk stratification when planning how and when to treat AAA.

The decision to treat an AAA is based on several factors, including the size of the aneurysm and comorbidities of the patient. AAAs can be managed medically if they are small (*watch and wait*), but when the risk of rupture outweighs the risk of treatment, they can be treated with open surgical repair or with the less invasive option of endovascular aortic repair. When the decision has been made to treat the aneurysm, there are two options, namely open surgical repair and EVAR. Open surgical repair (OSR) of AAA is a common and durable treatment option for patients with AAA; however, this invasive operation is associated with increased short-term morbidity and mortality.

EVAR, a less invasive alternative to OSR, employs a covered stent graft to exclude the aneurysmal sac from blood flow and pressure and prevent the walls of the aneurysm from further expanding and potentially rupturing. Nearly half of the aneurysms treated with EVAR do not regress, which continues to place the aneurysm at risk of rupture. This failure to regress, or continued sac expansion, can occur after EVAR either because of the natural history of the aneurysm disease process and the aneurysm*s failure to heal, or from Type II endoleaks (persistent filling and pressurization of the aneurysm sac that originates from collateral arteries that branch off of the aorta). Therefore, changes in dimension of the aneurysm sac should be monitored following EVAR. As changes in sac size occur in 3 dimensions, both changes in sac diameter and volume can be used to define aneurysm size according to the reporting standards for EVAR.
When the aneurysm sac continues to expand, whether or not associated with Type II endoleak, increased imaging surveillance is required. Often, continued aneurysm sac expansion results in a significant rate of secondary procedures, rehospitalizations, and an increased risk of all-cause mortality. The following points highlight the primary risks when the aneurysm sac fails to regress after EVAR:
• Sac expansion (> 5 mm) at 1 year was independently associated with late mortality, regardless of the presence or absence of endoleak. This data was obtained from all patients (n=2,437) undergoing EVAR between 2003 and 2011.
• A follow-up study using data from the full Vascular Quality Initiative between 2003 and 2017 from 14,827 patients found that patients with both expanding and stable sacs are at a greater risk of all-cause mortality, not aneurysm-related mortality. This affects the majority of EVAR patients, as the majority of aneurysms fail to regress (i.e., 60%).
• The ENGAGE global post market study between 2009 and 2011 of the world*s most commonly used stent graft, the Medtronic Endurant, showed again that sac expansion and stable sacs at one year were associated with an increase in late

mortality compared to those with sac regression.
• An analysis in 2020 of the latest data collected from the ENGAGE post market registry showed that patients with regressing sacs at 1 year had statistically significant better freedom from all-cause mortality and freedom from secondary endovascular reinterventions than patients with stable or expanding sacs.
• A recently published meta-analysis from 17,096 patients in the UK showed that patients without sac shrinkage, which was seen in 52% of all patients, had a significantly higher hazard of all-cause and AAA-related death, secondary intervention, late complications, and rupture.
• Real world data prospectively collected from 1997 through 2011 from 1,412 patients shows 35% to 50% of EVAR patients undergo secondary intervention within 2 to 5 years.
• At the recent public advisory meeting of the Circulatory System Devices Panel of the Medical Devices Advisory Committee hosted by the Food and Drug Administration (FDA) on November 2-3, 2021, a retrospective review of 1,835 EVARs performed between 2000-2016 from the University of Pennsylvania was presented. In this review, the overall re-intervention rate was 7.5%. Importantly, 55% of re-interventions were due to Type II Endoleak , and the most common cause of open conversions was sac expansion.

The need for reinterventions remains the Achilles heel of EVAR. However, there is strong evidence to show that sac regression is associated with reduced reintervention rates as well as aneurysm-related and cardiovascular morbidity and mortality. Strategies to increase the likelihood of sac regression will improve EVAR outcomes.

As mentioned above, reinterventions are EVAR*s weak spot. Endoleaks are the most frequent complications of EVAR and the main cause for clinical failure, with frequency reported rates ranging from 2.4 to 45.5%. Lifelong follow-up is necessary for patients who underwent EVAR, for monitoring of changes in sac size, possible undesirable side-effects (including endoleaks), and for the assessment of long-term success of EVAR. Computed tomography (CT) is commonly used for patient follow-up and is highly accurate in the detection of endoleaks.

CT imaging is used to monitor changes in aneurysm sac size and can be used to measure both diameter and volume. Diameter is commonly used to monitor changes in sac size. However, changes in sac volume are critically important as they indicate the long-term success of EVAR by taking into account that variations in size occur in 3 dimensions, and small changes in diameter may not reflect the overall change in shape of the aneurysm. Reconstructive volumetric measurement can be used to combine two-dimensional axial sections taken from different reference levels, and these section are then converted into a three-dimensional image to obtain volumetric measurements. Using volume analysis, Figure 3 (see protocol p. 23) shows that a 25 % increase in aneurysm volume can be associated with an insignificant increase in diameter (<5 mm), and diameter can vary greatly depending on the measurement technique and the choice of plane. Since volumetric measurements are three-dimensional, they are

able to detect minor changes compared to two-dimensional diameter changes. Two-dimensional measurements would be especially inadequate in areas with an irregular aneurysm wall. Therefore, both volume and diam

Study objective

The purpose of the pivotal study is to determine the safety and efficacy of IMPEDE-FX RapidFill for increasing the percentage of subjects with shrinkage of the abdominal aortic aneurysm sac when used as an adjunct to on-label EVAR stent graft treatment in subjects eligible for elective EVAR.

Study design

The clinical trial is a prospective, multicenter, randomized, pre-procedure, single-blind, open-label study. This study is a pre-procedure, single-blinded study, i.e. subjects are blinded to the treatment arm before the procedure; after the procedure, they will be unblinded prior to discharge to prevent unintentional unblinding due to imaging.
The randomized study has two arms, as described below:
- Treatment arm: Subjects in the treatment arm will have both an EVAR device and IMPEDE-FX RapidFill implants implanted.
- Control arm: Subjects in the control arm will have only an EVAR device implanted.
Subjects will be randomized in a 2:1 ratio (treatment: control).
In the treatment arm, a minimum of 10 grafts from each EVAR manufacturer (see procedural exclusion criteria #1 for details) must be used throughout the study.

Intervention

The procedure at which the Aortic Stent Graft (for the Control arm) and the IMPEDE-FX RapidFill System (for the Treatment arm) is considered the index procedure/treatment for this clinical trial. The IMPEDE-FX RapidFill System procedure will be completed under fluoroscopic guidance; refer to the corresponding device IFU regarding the specific steps for device access, deployment, and withdrawal.

Study burden and risks

Subjects enrolled in the trial will participate for a duration of 5 years with visits at 30 days, 6 months, 1 year and annually thereafter through 5 years after the index procedure.

Each potential subject will be evaluated as to whether they meet all of the inclusion criteria and none of the exclusion criteria for enrollment in the trial. Assessments included for screening/baseline assessment are those that

are generally done as part of standard of care.
The following screen/baseline assessments will be completed at the screening visit prior to the index procedure. All data from these assessments must be reported on the respective case report form.
• Demographic information
• Health Related Quality of Life Questionnaire
o Pre-procedure Dartmouth (*People Living with an Abdominal Aortic Aneurysm*)
o SF-12
• Medical history, including any risk factors.
• Physical exam, including abdominal and peripheral pulse examination.
• Contrast enhanced CT
o CT slice size: 1.5 mm or thinner
o CT characteristics: contrast
o Location: from the level of the diaphragm to the common femoral bifurcations
o Timing of the imaging: CT that is completed within 4 months of the index procedure.
• Blood count (CBC, creatinine, CRP)
o Timing: within 3 months maximum from the index procedure

The procedure at which the Aortic Stent Graft (for the Control arm) and the IMPEDE-FX RapidFill System (for the Treatment arm) is considered the index procedure/treatment for this clinical trial. The IMPEDE-FX RapidFill System procedure will be completed under fluoroscopic guidance; refer to the corresponding device IFU regarding the specific steps for device access, deployment, and withdrawal.
The following data (not an all-inclusive list) will be recorded on the respective Treatment Case Report Form:
• Total Endovascular time; from initial catheter introduction to last catheter removal
• Total IMPEDE-FX RapidFill procedure duration from catheter introduction to catheter removal (for the Treatment Arm)
• Anesthesia time
• Fluoroscopy time (contrast volume, time, radiation exposure)
• Contrast volume
• Access method and site
• Total radiation exposure
• Additional imaging
• Presence of intraprocedural endoleak, prior to IMPEDE-FX RapidFill Implant insertion (for the Treatment Arm) and at the conclusion of the index procedure
• Technical success
• Additional procedures performed during the index procedure, including type of device(s) used and reason for use
• Additional (ancillary) devices implanted/utilized during the index procedure that are related to the trial treatment
• Identification numbers for all investigational components
• Estimation of blood loss
• Procedural complications

• Time in ICU
A copy of the procedural angiogram may be requested by Shape Memory Medical.
Subjects who consent, are randomized into the treatment arm, have any part of the IMPEDE-FX RapidFill System introduced into their body but either treatment is not attempted or is unsuccessful (zero IMPEDE-FX RapidFill Implants inserted), will be considered *Intent to Treat* subjects. These subjects will be followed for 30-days for safety only, and thereafter per institutional standard of care. Intent to Treat subjects will count towards the total enrollment number of up to 180 subjects and will be included in the analysis of safety data.
If a subject is converted to open surgical repair at any point in the trial, and the IMPEDE-FX RapidFill Implants are removed, the subject will be followed for 30-days for safety only, and thereafter per institutional standard of care.

Subjects will be evaluated from the time that the IMPEDE-FX RapidFill System (for the Treatment Arm) and the endovascular graft (for the Control Arm) is implanted through hospital discharge. The following information will be captured on the respective CRF:
• Duration of hospital stay (in hours)
• Adverse event assessment
• Duration of intensive care unit after index procedure (in hours)
• Groin evaluation
• Abdominal examination
• Post-implantation Syndrome assessment
o CBC, temperature, CRP

Subjects will complete follow-up visits at 1 month (30 days ± 14 days), 6 months (180 days ± 4 weeks), 1 year (365 days ± 4 weeks), and annually thereafter through 5-years post procedure (± 4 weeks).
At each of these visits, the following will be obtained:
• Physical exam (including incision site assessment for the 1-month follow-up)
• Health Related Quality of Life Questionnaire
o Post-Procedure Dartmouth (*People who have had surgery to Repair an Abdominal Aortic Aneurysm*)
o SF-12
• CT scan with contrast will be obtained.
• Abdominal X-ray will be obtained (3 view KUB). Only required at the 1 year, 3 year, and 5 year visits.
• Duplex Ultrasound will be obtained.
In the case that a CT scan is performed before the 1-month follow-up, the first post-procedure CT can substitute for the 1-month CT, as long as it is acquired within 37 days.
Requirements of the CT imaging will be as follows:
• CT slice size: 1.0 mm or thinner
• CT characteristics: three-phase study (non-contrast, contrast, and delayed)
• Location: from the level of the diaphragm to the common femoral bifurcations
Based off of the CTA, at each of these visits, the following assessments will

be completed by both the site and Core Lab:
• Assessment for EVAR stent graft integrity (fracture) which will be evaluated by abdominal X-ray with at least 2 obliquities.
• Evaluation for the following:
o EVAR-related observations, including endoleaks, patency and migration (measured against the 30-day CT)
o Evaluation for IMPEDE-FX RapidFill Implant migration (implants outside of the aneurysm sac)
o Aneurysm diameter
o Graft limb patency
o Renal artery patency
Additionally, the following assessments will be completed by sites:
• Collection of any adverse event information.
• Post-implantation syndrome assessment at the 1-month visit.
o CBC, temperature
• C-reactive protein

After the index procedure, additional interventions may be needed that may be related to the Aortic Stent Graft, the IMPEDE-FX RapidFill System (for the Treatment Arm), and/or the underlying lesion. Information regarding these interventions will be captured on the respective CRF.
The following information regarding any secondary interventions completed will be captured:
• type of secondary intervention
• reason of secondary intervention
• time from index procedure
• collection of any adverse event information
• any device(s) used during the secondary intervention
If a subject requires explantation of the IMPEDE-FX RapidFill Implants, the subject will be followed for 30-days or until hospital discharge, whichever is longer, for safety and then will exit the trial.

If a subject returns for an unscheduled visit (i.e., between the protocol defined follow-up visits) regarding the treated aneurysm, the specific assessments completed will be at the discretion of the treating physician. The following will be documented on the respective CRF, as well as the following:
• Reason for unscheduled visit
• Date of the visit
The following additional information will be documented on the respective CRF, as applicable:
• Assessment of the Aortic Stent Graft, as well as the IMPEDE-FX RapidFill Implants (for the Treatment Arm)
• Evaluation for the following based on contrast enhanced CT and adjudicated by the Core Laboratory:
o Graft device-related observations, including endoleaks, and patency,
o Evaluation for Aortic Stent Graft and/or IMPEDE-FX RapidFill Implant migration
o Aneurysm diameter

o Graft limb patency
o Renal artery patency
• Collection of any adve

Contacts

Public
Shape Memory Medical

Ridder Park Drive 1321 Suite 10
San Jose CA 95131
US
Scientific
Shape Memory Medical

Ridder Park Drive 1321 Suite 10
San Jose CA 95131
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. >=18 years of age 2. A candidate for elective EVAR of an infrarenal fusiform aortic aneurysm >=5.5 cm in diameter in men and >= 5.0 cm in women 3. Thrombus burden (percentage of the AAA sac occupied by thrombus) <50%, based on pre-procedure CTA 4. Maximum Lumen diameter within the AAA sac of >=40mm 5. The predicted minimum number of IMPEDE-FX RapidFill Implants for the subject is <=200

Exclusion criteria

General 1. An inability to provide informed consent 2. Enrolled in another clinical study that could interfere with the outcomes being studied in this trial 3. Unable or unwilling to comply with study follow-up requirements 4. Prisoner or member of other vulnerable population

Anatomical 1. Concomitant iliac artery ectasia or aneurysm 2. Vascular disease and/or anatomy that preclude the safe access and positioning of a catheter to deliver the investigational product into the AAA sac 3. Ruptured, leaking, inflammatory or mycotic (infected) aneurysm 4. Connective tissue disorder (e.g., Marfan*s syndrome) 5. Aneurysmal disease of the descending thoracic aorta 6. Excessive calcification at the aortic bifurcation to common/internal iliac bifurcation, that might lead to access difficulties

EVAR/Procedural 1. Use of aortic stent grafts other than the Gore Excluder AAA Endoprosthesis, Gore Excluder Conformable AAA Endoprosthesis, Cook Zenith Flex AAA Endovascular Graft, Medtronic Endurant II and Endurant IIs Stent Graft, or the Terumo TREO Stent Graft to treat the AAA 2. Use of an aortic stent graft other than those specified2 for a particular site 3. Planned use of the chosen stent graft outside its IFU 4. Use of fenestrated stent grafts or chimney techniques 5. Use of the Heli-FX EndoAnchor system 6. Use of embolic devices other than the investigational product to embolize the AAA sac 7. Use of embolic products to prophylactically or concomitantly embolize the inferior mesenteric artery, lumbar arteries, renal accessory arteries, or internal iliac arteries 8. Inability to land the distal-most portion of the EVAR stent graft limbs, including extensions, above the internal iliac arteries

Medical History/Conditions 1. Coagulopathy or uncontrolled bleeding disorder 2. Serum creatinine level >2.5 mg/dL 3. Cerebrovascular accident within 3 months prior to the procedure 4. Myocardial infarction and/or major heart surgery within 3 months prior to the procedure 5. Atrial fibrillation that is not well rate controlled 6. Life expectancy of <2 years post-procedure 7. Known hypersensitivity or contraindication to platinum, iridium, or polyurethane 8. Have active infection at the time of the index procedure documented by pain, fever, drainage, positive culture, or leukocytosis (WBC >11,000/mm3) 9. A condition that inhibits radiographic visualization during the implantation procedure 10. History of allergy to contrast medium that cannot be managed medically, or subject is unable to have a CT with contrast for any reason 11. Uncontrolled co-morbid medical condition, including mental health issues, that would adversely affect participation in the trial 12. Pregnant or lactating female: for females of child-bearing potential, based on a positive pregnancy test within 7 days prior to the procedure or refusal to use a medically accepted method of birth control for the duration of the trial

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	20-10-2024
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Generic name:	IMPEDE®-FX RapidFill®
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO

Date:	19-11-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT0029660
CCMO	NL85738.000.24