SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Stent, Iliac Vein
Device Trade Name:	Abre Venous Self-expanding Stent System
Device Procode:	QAN
Applicant's Name and Address:	Medtronic Vascular, Inc. 3033 Campus Drive Plymouth, Minnesota 55441
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P200026
Date of FDA Notice of Approval:	October 21, 2020

II. INDICATIONS FOR USE

The Abre Venous Self-expanding Stent System is intended for use in the iliofemoral veins for the treatment of symptomatic venous outflow obstruction.

III. CONTRAINDICATIONS

The Abre Venous Self-expanding Stent System is contraindicated for use in:

- Patients with known hypersensitivity to nickel titanium (nitinol).
- Patients who are judged to have a lesion that prevents complete inflation of a balloon dilatation catheter or proper placement of the stent or the stent delivery system.
- Patients in whom anticoagulant or antiplatelet therapy is contraindicated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Abre Venous Self-expanding Stent System labeling (Instructions for Use).

V. DEVICE DESCRIPTION

The Abre Venous Self-expanding Stent System (Abre stent) consists of a stent and stent delivery system designed specifically for implantation in the peripheral venous system. The system consists of a flexible self-expanding stent made of a nickel-titanium alloy (nitinol) provided in multiple lengths and diameters and an over-the-wire stent delivery

system.

The Abre stent (Figure 1) is laser machined from a continuous seamless piece of nitinol tubing into an open lattice design. The stent includes three integral nitinol markers at each end to enhance visualization of the stent ends both before and after deployment.

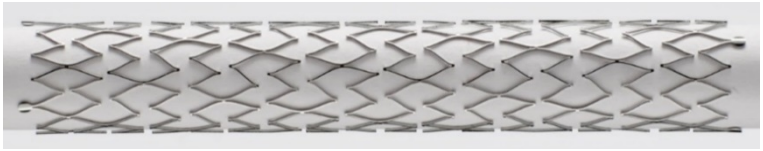


Figure 1. Abre Stent

The Abre stent matrix consists of stent diameters ranging from 10-20 mm and stent lengths ranging from 40-150mm. The Abre Venous Self-expanding Stent System size matrix is provided in Table 1.

Table 1. Abre Stent Diameters and Lengths

		Stent Length (mm)					
		40	60	80	100	120	150
Stent Diameter (mm)	10	x	x	x	x	x	x
	12		x	x	x	x	x
	14		x	x	x	x	x
	16		x	x	x	x	x
	18		x	x	x	x	x
	20		x	x	x	x	x

The Abre delivery system (Figure 2) is an over-the-wire (OTW), 9 Fr, 0.035" guidewire compatible, delivery system for deploying the Abre stent. The delivery system is a single configuration used for deployment of all stent sizes. The Abre delivery system consists of a single use, disposable triaxial shaft catheter with a handle containing a thumbwheel-actuated deployment mechanism, providing control and accuracy during stent placement. A locking pin prevents the stent from being deployed prior to use and must be removed to actuate the thumbwheel. A single luer port is located on the proximal end of the deployment handle to allow for saline to be injected to flush air from the system.

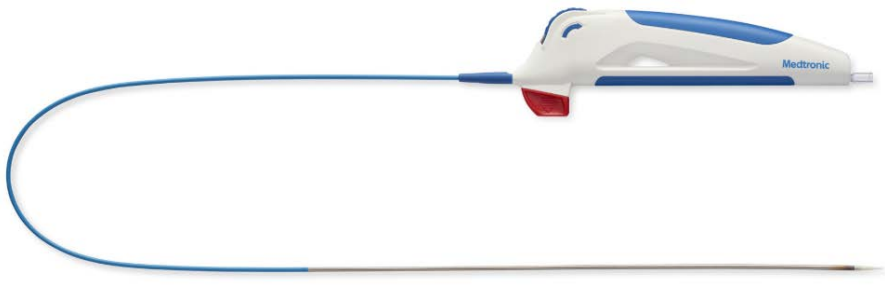


Figure 2. Abre Delivery System

Upon gaining access to the patient vasculature with an introducer sheath and guidewire, the target vessel is dilated with an appropriately sized balloon per the Abre instructions for use (IFU). Next, the Abre delivery system is introduced over the guidewire through the hemostatic valve and introducer sheath. The Abre delivery system is advanced through the vasculature until the leading edge of the stent extends beyond the target lesion. The Abre stent is then deployed by removing the lock pin from the delivery system handle and rotating the thumbwheel until the stent is fully deployed. Upon release of the stent at the target lesion, the stent expands and conforms to the vessel wall.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives used in the treatment of symptomatic iliofemoral venous outflow obstruction. Non-interventional management consists of compression therapy, elevation of the extremity, and anticoagulation. In the setting of acute deep vein thrombosis (DVT), active thrombus removal techniques such as pharmacologic thrombolysis and percutaneous mechanical thrombectomy in combination may be employed. Post-thrombotic and non-thrombotic iliofemoral outflow obstruction, or underlying obstruction after acute thrombus removal in the setting of acute DVT, may be treated with venous angioplasty and stenting to re-establish venous patency with another approved stent. Open surgical treatments are also available, including endophlebectomy or bypass.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Abre Venous Self-expanding Stent System has been commercially available outside the US since April 2017. It was first marketed in the European Union (EU) and has been commercialized in Argentina, Australia, Colombia, Costa Rica, Ecuador, Guatemala, Honduras, India, Israel, New Zealand, Peru, Russia, Saudi Arabia, Singapore, Turkey, Ukraine, and Vietnam.

The Abre Venous Self-expanding Stent System has never been withdrawn from any market as a result of risk of serious adverse health consequences or for any reason related to safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Access failure
- Access site infection
- Allergic reaction to contrast medium or procedure medications

- Allergic reaction to nitinol or other device materials
- Aneurysm
- Arteriovenous (AV) fistula
- Bleeding
- Bruising
- Death
- Device breakage
- Device maldeployment
- Edema
- Embolization
- Fever
- Hematoma
- Hypertension
- Hypotension, nausea, or other vasovagal response
- Infection
- Myocardial infarction, arrhythmia, or other cardiovascular insufficiency
- Open surgical repair
- Pain
- Pseudoaneurysm
- Renal insufficiency or renal failure (new or worsening)
- Respiratory distress or pulmonary embolism
- Sepsis
- Stent fracture
- Stent malapposition
- Stent malposition
- Stent migration
- Stroke, paradoxical embolism, transient ischemic attack, or intracerebral hemorrhage
- Tissue necrosis
- Venous occlusion, restenosis, or thrombosis, within or outside of stented segment
- Vessel damage, including intimal injury, dissection, perforation, or rupture

For the specific adverse events that occurred in the clinical study, see Section X below.

IX. SUMMARY OF NON-CLINICAL STUDIES

A series of non-clinical laboratory and animal studies related to the product were performed to evaluate the device.

A. Biocompatibility Studies

Biocompatibility testing was performed in accordance with ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process" and FDA guidance document "Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems" to demonstrate that the components of the Abre Stent and Abre Delivery System are biocompatible. Test samples were manufactured in accordance with standard operating procedures, subjected to two cycles of ethylene oxide sterilization, and are representative of finished product.

The stent and delivery system were categorized per ISO 10993-1 based on the intended patient contact and duration. The stent is permanently implanted in the patient's vasculature and therefore has permanent (>30 days) circulating blood contact. The delivery system catheter, which is not implanted, is categorized as external communicating with limited (<24-hour) circulating blood contact duration.

Based on the results of chemical characterization testing and toxicological risk assessments of the stent and the delivery system, subacute/subchronic and chronic toxicity, genotoxicity and carcinogenicity testing were not conducted on the stent and genotoxicity testing was not conducted on the delivery system.

The endpoint of thrombogenicity for the stent and the delivery system was assessed in the GLP safety study, as outlined in Section F. In addition to the implantation assessments per ISO 10993-6, the implantation endpoint of the stent was also assessed in the GLP safety study, as outlined in Section F.

The tests summarized in Table 2, which passed requirements, were conducted in support of the Abre Stent and the Abre Delivery System, as indicated.

Table 2. Summary of Biocompatibility Evaluation for the Abre Venous Self-expanding Stent System

Test	Test Description/ Applicable Standard	Stent	Delivery System	Results
Cytotoxicity	L929 MEM Elution ISO 10993-5:2009, Tests for in vitro cytotoxicity	X	X	Non-cytotoxic
Sensitization	Guinea Pig Maximization ISO 10993-10:2010, Tests for irritation and sensitization	X	X	Non-sensitizing
Irritation or Intracutaneous Reactivity	Intracutaneous Reactivity ISO 10993-10:2010, Tests for irritation and sensitization	X	X	Non-irritant
Systemic Toxicity (Acute)	Acute Systemic Toxicity ISO 10993-11:2006, Tests for systemic toxicity	X	X	Non-toxic
Material Mediated Pyrogenicity	Material Mediated Pyrogenicity ISO 10993-11:2006, Tests for systemic toxicity	X	X	Non-pyrogenic
Implantation	Intramuscular Implantation ISO 10993-6:2007, Tests for local effects after implantation	X	N/A	Non-irritant
Hemocompatibility	Hemolysis Direct and Indirect Contact ASTM F756	X	X	Non-hemolytic
	Complement Activation (C3a and SC5b-9) ISO 10993-4: 2002, Selection of tests for interactions with blood, as amended 2006	X	X	Non-activator of the complement system
	Thrombogenicity (In Vivo) ISO 10993-4: 2002, Selection of tests for interactions with blood, as amended 2006	N/A	X	Acceptable thrombogenic performance in the presence of anticoagulation
Chemical Characterization by NVR, LC-MS, GC-MS, and ICP-MS and Toxicological Assessment	ISO 10993-17: 2002, Establishing allowable limits for leachable substances ISO 10993-18: 2005, Chemical Characterization of materials	X	X	Overall assessment demonstrated that the extractables/ leachables are not a concern for subacute/ subchronic/ chronic systemic toxicity, genotoxicity, or carcinogenicity.

B. Laboratory Studies

In vitro bench testing was conducted as part of the design verification and validation to support the safety and effectiveness of the Abre Venous Self-expanding Stent System.

The testing and results summarized in Table 3 are reflective of requirements per FDA and internationally-recognized standards. Table 3 includes both non-aged (T=0) and 3-year accelerated aging (indicated by "*") testing.

Table 3. Summary of *In Vitro* Bench Testing

<table>
<tr><th>Test</th><th>Test Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td colspan="4">Stent Testing</td></tr>
<tr><td>Raw Material Composition</td><td>To evaluate the stent material composition</td><td>Material composition must comply with ASTM F2063-12 and ASTM F2063-05</td><td>Stent material conforms to material standards.</td></tr>
<tr><td>Austenite Finish (A_f) Temperature Testing</td><td>To measure the temperature at which a compacted stent achieves full self-expansion (A_f Temperature)</td><td>The stent shall have an active Austenite finish temperature in the range of 14-24 degrees Celsius.</td><td>PASS</td></tr>
<tr><td>Kink Resistance</td><td>To assess stent kinking in vessels with high curvature.</td><td>The stent shall bend to a radius ≤1.0in without kinking.</td><td>PASS</td></tr>
<tr><td>Stent Integrity*</td><td>To evaluate the ability of stent to achieve full self-expansion post deployment and resist delivery-related damage.</td><td>Following deployment, the unconstrained stent shall expand to nominal inner diameter and length, and also be free of visible defects related to delivery.</td><td>PASS</td></tr>
<tr><td>Stent Visibility /Radiopacity</td><td>To evaluate radiopacity of stent for visibility during and after device delivery.</td><td>The stent marker shall provide a minimum radiopacity of 52% and a minimum cross-sectional viewing area of 0.596mm^2.</td><td>PASS</td></tr>
<tr><td>Flexibility</td><td>To evaluate stent flexibility by measuring its resistance to bending under a three-point bend loading mode.</td><td>The slope of the bending force-displacement curve using a three-point bend fixture must be less than:
<table>
<tr><th>Stent Diameter (mm)</th><th>Slope Maximum (N/mm)</th></tr>
<tr><td>10</td><td>0.057</td></tr>
<tr><td>12</td><td>0.108</td></tr>
<tr><td>14</td><td>0.174</td></tr>
<tr><td>16</td><td>0.171</td></tr>
<tr><td>18</td><td>0.201</td></tr>
<tr><td>20</td><td>0.167</td></tr>
</table></td><td>PASS</td></tr>
<tr><td>Stent Recovered Inside Diameter (Dimensional Verification)</td><td>To determine whether the stent expands to the correct diameter following deployment.</td><td>The unconstrained stent diameter after deployment must be ±4% from the labeled diameter.</td><td>PASS</td></tr>
</table>

Test	Test Purpose	Acceptance Criteria	Results
Stent Contact Area	To determine the percent contact area of a deployed stent with the vessel wall.	Contact area of the stent is to be measured or calculated and reported as percent surface area.	12-18%
Foreshortening*	Measures the difference between the stent length in the delivery system and the stent length when deployed in a target vessel.	The deployed stent length in a representative path shall be equal to or less than 10 percent, or equal to or less than 5mm different than the stent length in the delivery system, whichever is greater.	PASS
Normalized Lateral Stiffness (NLS) Minimum	To measure the resistance of the expanded stent to lateral compression as a function of normalized stiffness (NLS).	The minimum normalized lateral stiffness (NLS) for all stent sizes shall be 0.157N/mm.	PASS
Normalized Lateral Stiffness (NLS) Maximum		The maximum normalized lateral stiffness (NLS) for all stent diameters shall be 0.294N/mm.	PASS
Radial Force: Radial outward loading and unloading*	To measure the resistive force of the stent to radial compression, simulating before (unloading) and after (loading) balloon dilation within the vessel.	The radial outward loading force (radial strength) minimum shall be 0.079N/mm and maximum shall be 0.403N/mm. The radial outward unloading force (radial strength) minimum shall be 0.026N/mm.	PASS
Radial Force: Unloading at maximum vessel diameter (at deployment and life of device)*		The unloading radial strength at maximum implanted vessel diameter shall be greater than 0.027N/mm.	PASS
Particulate Evaluation	To measure the size and number of the particulate shed by the stent and delivery system.	Post-sterilization and distribution, the stent and delivery system must not shed particulate that exceed 6000/10µm and does not exceed 600/25µm per USP 788.	PASS
Mechanical Properties	Characterization testing performed to determine tensile and fatigue properties as inputs to support stress/strain and fatigue analysis.		
Finite Element Analysis	Characterization testing performed to determine maximum stresses and strains within the device to support fatigue analysis.		
Endurance Limit Analysis	To determine the safety factor of the stent at relevant fatigue failure modes, and determine which modes require physical testing.	All safety factors > 1.0. Worst case testing to be performed for any safety factor < 2.0.	PASS

Test	Test Purpose	Acceptance Criteria	Results
Accelerated Durability Testing	Evaluate the durability of the stent after a period of 10 years and 50 years.	The stent must withstand an equivalent of 10 years and 50 years of accelerated durability testing without Type III, Type IV or Type V fractures.	PASS The stent showed no Type III, Type IV or Type V strut fractures after 10 years and 50 years of accelerated durability testing.
MRI Safety and Compatibility	To evaluate stent safety and compatibility with MRI.	The conditions under which the device can be safely scanned are determined for product labeling.	The stent is MR Conditional at a field strength of 1.5T and 3.0T
Corrosion Resistance	To evaluate the potentiodynamic corrosion resistance of the stent.	The measured breakdown potential (E_B) must be at least 200mV greater than the resting potential (E_R).	PASS
Nickel-ion Release	To characterize general/uniform corrosion resistance of the stent.	Stent should exhibit low nickel ion release rate over 60-day period.	Nickel ion release rate over a 60-day period was 0.073 µg/day. The peak nickel ion release rate in one day was 2.13µg/day.
Delivery System			
Working Length*	Measures the length of the delivery system catheter.	The delivery system working length shall be 90 cm +/- 4.5 cm.	PASS
Dimensions: Overall Length*	Measures the length of the device.	Overall length of the device shall be 116cm +2cm/-4cm.	PASS
Dimensions: Lumen ID*	Measures the delivery system lumen ID to ensure compatibility with a .035" guidewire.	Shall be able to insert and withdraw a mandrel with minimum diameter of 0.0360 inch.	PASS
Dimensions: Crossing Profile*	Measures the crossing profile to ensure fit in a 9Fr introducer sheath.	Crossing profile must be ≤0.122 inches.	PASS
Tensile: Distal Tip to Tip Tube*	Measures the distal tip to tip tube bond strength.	The distal tip to tip tube bond must withstand ≥3.8 lbf.	PASS
Tensile: Luer to Tip Tube*	Measures the luer to tip tube bond strength.	The luer hub to tip tube bond must withstand ≥3.8 lbf.	PASS
Tensile: Luer to Stop Tube*	Measures the luer to stop tube bond strength.	The luer hub to stop tube bond strength must withstand ≥3.8 lbf.	PASS
Tensile: Outer Clip to Pull Cable*	Measures the outer clip to pull cable bond strength.	The outer clip to pull cable bond must withstand ≥12.6 lbf.	PASS
Tensile: Thumbwheel to Pull Cable*	Measures the thumbwheel to pull cable bond strength.	The thumbwheel to pull cable bond must withstand ≥12.6 lbf.	PASS
Tensile: Isolation Sheath to Handle*	Measures the isolation sheath to handle bond strength.	The isolation sheath to handle bond must withstand ≥3.37 lbf.	PASS

Test	Test Purpose	Acceptance Criteria	Results
Markerband Visibility	Measures the radiopacity and cross-sectional viewing area of the markerband.	The markerband must provide a minimum radiopacity of 64% and a minimum cross-sectional viewing area of 1.62mm^2.	PASS
Tip Visibility	Measures the radiopacity of the tip.	The radiopacity of the tip must be 65±10%.	PASS
Guidewire Loading Success*	Verifies the ability to insert and track the delivery system over a 0.035-inch guidewire.	Must be able to insert and track the delivery system over a 0.035-inch guidewire 3x in a representative path.	PASS
No Pre-deployment*	Verifies the ability of the delivery system to maintain stent coverage after tracking.	The delivery system shall be able to maintain stent coverage without pre-deployment after tracking through a representative model.	PASS
Deployability*	Confirms successful deployment.	Shall be able to successfully deploy a stent from the delivery system while placed in a representative model, and meet deployment force of equal to or less than 4.0 lbf	PASS
Tracking and withdrawal*	Verifies the delivery system remains intact after insertion and withdrawal.	Must be able to insert and remove delivery system from sheath over a guidewire in a representative path with the delivery system remaining fully intact after withdrawal.	PASS
Withdrawal*	Verifies the ability of the delivery system to be removed without dislodging the stent.	Must be able to remove delivery system without stent motion or dislodgement.	PASS
Deployment Force*	Measures the force required to deploy the stent.	The wheel actuation force applied to thumbwheel required to deploy stent shall be equal to or less than 4.0 lbf	PASS
Lock Pin Removal Force	Measures the force required to remove the lock pin.	Lock pin removal force must be ≤8.1 lbf.	PASS
Flushing*	Verifies the ability to flush the guidewire lumen.	Ability to flush guidewire lumen using maximum of 10cc of saline	PASS
Delivery System Freedom from Leakage*	Evaluates the delivery system for leakage.	The delivery system should be evaluated for leakage by flushing with water and no leaks are observed.	PASS
3x Tracking Force*	Measures the force required to track the delivery system through the vasculature.	The force required to track the delivery system through a representative model shall be equal to or less than 4.0 lbf.	PASS

Test	Test Purpose	Acceptance Criteria	Results
Deployment: Initial Flower to Final Position*	Measures the distance the stent moves upon deployment of the stent.	The movement of distal end of stent from initial flower to final deployment shall be less than or equal to 3mm.	PASS
Deployment: Proximal Edge of marker band to final position*		The distance from initial location of marker band to final location of stent shall be less than or equal to 5mm without repositioning.	PASS
Particulate Evaluation	Measures the particulate shed by the stent and delivery system.	Post-sterilization and distribution, the delivery system must not shed particulate that exceed 6000/10µm and does not exceed 600/25 per USP 788.	PASS
Delivery System Kink*	Evaluates the flexibility and kink of the delivery system.	The delivery system is evaluated for flexibility and kink performance using progressively tighter radius curves and characterized at the point at which the system starts to kink.	PASS
Delivery System Torque*	Evaluates the torque strength of the delivery system.	The delivery system is evaluated for torque strength by continually rotating 180 degrees until failure occurs.	PASS

*Denotes testing also conducted for 3-year accelerated aging.

C. Packaging

Packaging verification testing was performed at non-aged and aged conditions to demonstrate integrity of the packaging is maintained over the shelf-life of the device. Testing, which passed pre-determined requirements, included a visual assessment, dye penetration testing, bubble leak testing, and seal strength testing.

D. Shelf-life

Shelf life testing of the device (assessed by the tests denoted with an asterisk in Table 3) and of packaging passed pre-determined requirements. Testing was performed to support a 3-year shelf life.

E. Sterilization

The Abre Venous Self-expanding Stent System is a single-use device. The device is terminally sterilized using 100% ethylene oxide (EO) gas. In accordance with AAMI/ANSI/ISO 11135, "Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices", sterilization testing was performed on the Abre Venous Self-expanding Stent System to demonstrate that the device can be adequately sterilized to the desired Sterility Assurance Level (SAL) of 10^{-6}. Ethylene Oxide and Ethylene Chlorohydrin residuals meet the requirements of ISO 10993-7, "Biological

Evaluation of Medical Devices – Part 7: Ethylene oxide sterilization residuals".

F. Animal Studies

Three GLP and one non-GLP animal studies were conducted to evaluate the acute handling and performance and the chronic safety of the Abre Venous Self-expanding Stent System. The *in vivo* animal studies demonstrated the safety and overall performance of the Abre Venous Self-expanding Stent System. Table 4 provides a summary of the animal studies performed.

Table 4. Summary of Animal Studies

Study	28-Day GLP Migration Study
Study Purpose	Evaluate migration of the Abre stent at 28-days post-implant
Study Summary and Results	This study was designed to assess the migration of the Abre stent compared to a control stent at 28 days post-implant in a domestic swine animal model. The study met all success criteria with no safety risks identified. All animals survived to the respective 28-day timepoint and were observed to be clinically healthy through the study duration. There were no test or control article malfunctions or adverse events that occurred during the study. The Abre stent demonstrated favorable results compared to the control regarding migration and equivalent performance in regard to stenosis. No stent fractures were observed. The stent sizes chosen were to allow for a 0-10% stent oversizing based upon the outside diameter of the stent. Overall, there was a high correlation with increased stent diameter relative to the native vessel size causing disruption of the venous wall architecture or integrity which induced increased neointimal hyperplasia with resultant increased percent stenosis for both the Abre stent and the control stent. However, even though the Abre stent exhibited a greater average stent diameter than the control stent, the Abre venous stent frequently had equivalent or less percent stenosis and mean neointimal thickness in the animal matched groups. The pathology findings of the study were supportive of an acceptable safety profile for the Abre stent.
Study	28-Day GLP Safety Study
Study Purpose	Evaluate the safety of the Abre stent at 28-days post-implant
Study Summary and Results	This study was designed to evaluate the safety of the Abre stent compared to a control stent at 28 days post-implant in a domestic swine model. The study met all success criteria with no safety risks identified. The Abre stent and the control stents were implanted in a single configuration and in an overlapped configuration. Nineteen of the twenty animals survived to the respective 28-day timepoint and were observed to be clinically healthy through the study duration. One animal was terminated early due to morbidity unrelated to a test device (animal experienced a femur fracture due to a fall during transport). There were no Abre or control device malfunctions or adverse events that occurred during the study. There were no incidents of stent fractures in the Abre stent; the control stent had one Type I fracture. Overall, Abre slightly outperformed the control for percent stenosis in both the single and overlapped configurations. There was a high correlation with increased stent diameter causing disruption of the venous wall architecture or integrity which induces increased neointimal hyperplasia with resultant

	increased percent stenosis for both the Abre stent and the control stent. However, even though the Abre stent exhibited a greater average stent diameter than the control stent, the Abre stent consistently had equivalent percent stenosis and mean neointimal thickness. The pathology findings of the study were supportive of an acceptable safety profile for the Abre stent in single and overlapping configurations.
Study	Acute GLP Animal Study
Study Purpose	Evaluate the acute performance and handling of the Abre Venous Self-expanding Stent System
Study Summary and Results	This study was designed to assess the acute performance and handling of the Abre Venous Self-expanding Stent System in a domestic swine animal model. The stent sizes were selected by the implanting physicians based on the estimated vein diameters and the device sizing tables. Fluoroscopy and intravascular ultrasound (IVUS) were used for procedural support and data collection. Performance and handling assessments were performed by two external physicians experienced in venous stenting for each stent that was deployed. Product and performance requirements related to the stent, delivery system compatibility, use of the device in a procedure, and packaging/labeling were evaluated by the physicians on a 1-5 rating scale. Following the final stent implantation, each animal was humanely euthanized and transferred to necropsy for a gross evaluation. Vascular trauma, site specific thrombogenicity, and overall thromboembolism on downstream circulation and downstream end organs were evaluated. The Abre Venous Self-expanding Stent System met all acceptance criteria in the physician assessments. There were no signs of site-specific thrombus formation for any stent, and no signs of potential thromboembolism in any animal. Some degree of vascular trauma was observed, however it was rated as “minimal to mild”. In addition, vessel injury scores were comparable between the Abre stent and the control stent. The study results from physician feedback and pathology results demonstrated that the Abre Venous Self-expanding Stent System performed as intended and met all defined acceptance criteria for evaluation requirements.
Study	180-day Non-GLP Study
Study Purpose	Assess the safety of the Abre stent at 180 days post-implant
Study Summary and Results	This study was designed to assess the safety of the Abre stent compared to a control stent at 180 days post-implant in a domestic swine animal model. The study met all success criteria with no safety risks identified. All animals survived until their scheduled 180-day timepoint and no major acute and/or sub-acute complications during implant and throughout in-life were experienced. Clinically, all animals experienced some degree of post procedural pain demonstrated by lameness and abnormal posture. This was likely the result of outward migration of the struts, causing compression on perivascular spaces/organs (e.g. sensory nerve fibers) where there is minimal connective tissue present in the domestic swine model. Symptoms of pain resolved quickly in all cases. There were no device or procedure related adverse events for either test or control articles. In all evaluated sites, virtually all stent struts were residing in the perivascular connective/adipose tissue space and were not directly abutting the medial wall of the vein and

	there was marked disruption of venous wall architecture or integrity. All struts were surrounded by connective tissue extending from the venous adventitia and invariably associated with inflammation and/or fragments of tunica media. Overall, there was a high correlation with increased stent diameter inducing increased neointimal hyperplasia with resultant increased percent stenosis for both the Abre stent and the control stent. In addition, the control stent exhibited a higher incidence of more severe para-strut and neointimal inflammation than the Abre stent.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study (ABRE Study) to establish a reasonable assurance of safety and effectiveness of iliofemoral venous stenting with the Abre Venous Self-expanding Stent System for symptomatic iliofemoral venous outflow obstruction under IDE G160163. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The ABRE Study was a prospective, interventional, non-randomized, single-arm, multicenter, global study, with each center following a common protocol. Safety and effectiveness were designed to be evaluated against performance goals developed from the scientific literature. A Statistical Analysis Plan (SAP) was followed for the ABRE Study.

Subjects were treated between December 19, 2017 and November 29, 2018. The database for this PMA reflected data collected through January 17, 2020, the data cut-off date. Subjects were categorized as acute DVT, post-thrombotic syndrome (PTS), or non-thrombotic iliac vein lesion (NIVL), for a total of 200 subjects who were implanted with at least one Abre stent at 24 investigational sites in the US and Europe (France, Germany, Ireland, Italy, and United Kingdom).

Subjects in the ABRE Study were evaluated at a screening visit, during the index procedure, through hospital discharge, and then at 30 days, 6 months, and 12 months post-procedure. ABRE Study subjects will continue to be followed through 24 months and 36 months post-index procedure.

Endpoint-related safety events were adjudicated by an independent Clinical Events Committee (CEC) according to the CEC manual of operations (MOP), and an independent Data Safety Monitoring Board (DSMB) ensured the well-being of the participants of the study and the continued validity and scientific merit of the study, per a DSMB Charter.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the ABRE Study was limited to patients who met the following inclusion criteria:

General Inclusion Criteria

1. Patient is ≥ 18 and ≤ 80 years of age;
2. Patient has at least one of the following clinical manifestations (i.e. symptoms and/or signs) of venous disease in lower extremity:
   a. Clinical-Etiological-Anatomical-Pathophysiological (CEAP) score ≥ 3
   b. Venous Clinical Severity Score pain score (VCSS) ≥2
   c. Suspected deep vein thrombosis (DVT);
3. Patient is willing and capable of complying with specified follow-up evaluations at the specified times;
4. Patient has been informed of the nature of the study, agrees to its provisions and has provided written informed consent, approved by the appropriate Ethics Board.

Imaging-based Inclusion Criteria

5. Patient has diagnosis of non-malignant venous obstruction within the common iliac, external iliac, and/or common femoral vein. The proximal point of the obstruction may extend to the iliac venous confluence of the inferior vena cava and the distal point may be at or above the deep femoral vein. Diagnosis must be made based on objective imaging by using venography and/or intravascular ultrasound (IVUS). Patient must have good inflow involving either the femoral or deep femoral vein being patent and at least a caudal section of the common femoral vein that is free of significant disease;
6. Patient has an obstructive lesion defined as:
   i. Occluded, or
   ii. ≥50% in diameter reduction on venography or IVUS, or
   iii. ≥50% area reduction on IVUS
7. Acute DVT patients should be treated with the Abre stent within 14 days after onset of symptoms. Patients with acute DVT must first undergo successful treatment of acute thrombus; successful treatment is defined as 30% or less residual thrombus by venogram, as determined by physician, no bleeding, no symptomatic pulmonary embolism (confirmed by imaging), and no renal compromise (renal compromise defined as glomerular filtration rate (GFR)<30). Patients with underlying obstructive lesions can then be included in the study within the same procedure;
8. Target vessel can accommodate a 9F Sheath, from insertion site to target segment;
9. Exchangeable guidewire must cross target lesion(s) with successful predilation.

Patients were <u>not</u> permitted to enroll in the ABRE Study if they met any of the following exclusion criteria:

General Exclusion Criteria

1. Patient with DVT in the target limb of which the onset of symptoms is

between 15 days and 6 months prior to planned treatment or patient has an acute DVT anywhere else than in the target vessel;

2. Patient has peripheral arterial disease-causing symptoms in target limb;
3. Patient is pregnant (female patients of child-bearing potential must have a pregnancy test done within 7 days prior to the index procedure);
4. Patient has a known or suspected systemic infection at the time of the index procedure;
5. Patient has a planned percutaneous or surgical intervention within 30 days prior or 30 days following index procedure, or a contralateral iliofemoral lesion requiring planned treatment within 12 months;
6. Patient requires femoral endovenectomy and patch venoplasty, greater saphenous vein ablation, and/or small saphenous vein stripping during the index procedure;
7. Patient has an active vasculitic inflammatory disorder (e.g. Behcet disease) predisposing the patient to thrombosis and requiring systemic corticosteroid therapy;
8. Patient has impaired renal function (GFR < 30) or is on dialysis;
9. Patient has a platelet count < 50,000 cells/mm3 or > 1,000,000 cells/mm^3 and/or a white blood cell count (WBC) < 3,000 cells/mm^3 or > 12,500 cells/mm^3;
10. Patient has a history of bleeding diathesis or either a history or presence of heparin-induced thrombocytopenia antibodies;
11. Patient has a known hypersensitivity or contraindication to antiplatelets or anticoagulation, nitinol, or a contrast sensitivity that cannot be adequately pre-medicated;
12. Patient has presence of other severe co-morbid conditions, which in the investigator's opinion may interfere with the patient's compliance with study visits and procedures, or may confound interpretation of study data (e.g. congestive heart failure Class III and IV, non-ambulatory patients, severe hepatic dysfunction, life expectancy < 1 year);
13. Patient belongs to a vulnerable population per investigator's judgment or patient has any kind of disorder that compromises his/her ability to give written informed consent and/or to comply with study procedures. Patient must be able to consent for themselves;
14. Patient is currently participating in another investigational drug or device study or observational competitive study.

Imaging-based Exclusion Criteria

15. Patient has a vena cava obstruction or lesion extending into the inferior vena cava (IVC), or the presence of bilateral iliofemoral venous lesions requiring planned treatment within 12 months;
16. Patient has significant venous bleeding, arterial dissection or other injury requiring additional percutaneous or surgical intervention prior to enrollment;
17. Patient has a previously placed stent in the ipsilateral venous vasculature;
18. Patient has disease that precludes safe advancement of the venous stent to

the target lesion(s).

2. Follow-up Schedule

All subjects underwent a clinical evaluation at screening (prior to index procedure); treated subjects underwent a clinical evaluation prior to hospital discharge. All ABRE Study subjects were scheduled to return for follow-up examinations at 30 days, 6 months, and 12 months post-index procedure. Subjects will continue to be followed at 24 months and 36 months post-index procedure. Clinical and imaging follow-up are performed at these timepoints to enable reporting of endpoints related to primary patency, acute success, target lesion revascularization, stent fractures, quality of life, and major adverse events (MAEs). All adverse events and complications were recorded at all visits through the 12-month evaluation. All adverse events and MAEs will continue to be reported through 36 months post-index procedure. Table 5 provides the follow-up schedule and evaluations required through the 36-month visit.

Table 5: Schedule of Assessments and Visit Windows

Data Collection Requirement	**Screening/Baseline (<30 days before procedure unless otherwise specified)**	**Procedure**	**Hospital Discharge**	**30 Day (-7/+14 days)**	**6 Months (± 30 days)**	**12 Months (± 30 days)**	**24 & 36 Months (± 30 days)**	**Unscheduled visit for intervention in target vein**
Informed Consent	X							
Demographics, Medical History & Physical Examination	X							
Pregnancy Test[1]	X							
Serum Creatinine, CBC	X							
INR (if on warfarin)	X			X	X	X	X	X
CEAP Classification	X							
Physical Assessment of Limbs	X		X	X	X	X	X	X
Villalta Score, VCSS	X			X	X	X	X	X[2]
VEINES-QOL/Sym, EQ-5D QOL	X				X	X	X	X[2]
Medication[3]	X	X	X	X	X	X	X	X
Document Adverse Events	X[4]	X	X	X	X	X	X	X
Duplex Ultrasound (DUS)	X		X[5]	X	X	X[6]	X	X
Procedure Data		X						X
Venogram	7	X[7,8]				6		X
IVUS	7	X[7,8]						X
Document Device Deficiencies		X	X	X	X	X	X	X

Data Collection Requirement	Screening/Baseline (<30 days before procedure unless otherwise specified)	Procedure	Hospital Discharge	30 Day (-7/+14 days)	6 Months (± 30 days)	12 Months (± 30 days)	24 & 36 Months (± 30 days)	Unscheduled visit for intervention in target vein
X-ray				9		X	X	X[10]
Discontinuation Information[11]			X	X	X	X	X	X

[1] Pregnancy test was required for women of child-bearing potential only to be completed within 7 days prior to the index procedure.

[2] Assessments and questionnaires were required prior to any intervention.

[3] Medications collected: Antithrombotics, Antibiotics, Immunosuppressants, NSAIDs, Steroids, Diuretics, Calcium-channel blockers, Statins.

[4]Adverse Event assessments were completed as of the moment the subject signed and dated the informed consent form.

[5]The DUS examination immediately after the index procedure was required to be performed between 0 and 7 calendar days from the index procedure.

[6]An additional venogram was required when:

(1) DUS assessment was suggestive of ≥50% restenosis or occlusion per investigator assessment, or;

(2) DUS was non-diagnostic or suboptimal such as when a subject was obese (e.g. with a BMI >40), or;

(3) was clinically required, or in other words when the subject had symptoms of venous disease in the target limb requiring a venogram.

[7]Diagnosis was made during the screening/baseline prior to the index procedure based on objective imaging using venography or IVUS.

[8]Required pre-stenting and post-stenting

[9]X-rays at 30 days were performed on the first 30 included subjects only for the first safety analysis (i.e. stent fracture).

[10]Plain x-ray was required pre and post re-intervention to assess for stent fracture.

[11] The discontinuation information was required whenever the subject ended involvement in the study.

All subjects were required to undergo duplex ultrasound (DUS) assessments for determination of the primary effectiveness endpoint of primary patency at 12 months. An additional venogram was required when the DUS assessment was suggestive of ≥50% restenosis or occlusion per investigator assessment, or when the DUS was non-diagnostic or suboptimal, or when the venogram was clinically required. In cases where both DUS and venography from the 12-month visit were available, venography was used for the primary patency assessment.

3. Clinical Endpoints

Primary safety endpoint

The primary safety endpoint was the incidence of composite MAEs at 30 days following stenting of an obstruction in the iliofemoral venous segment. MAEs were adjudicated by a CEC, except for stent thrombosis and stent migration, which were confirmed by core laboratory.

The components of the 30-day MAE composite include:

- All-cause death occurring post-procedure
- Clinically significant pulmonary embolism (i.e., symptomatic,

confirmed by CT pulmonary angiography)
- Major bleeding complication (procedural)
- Stent thrombosis confirmed by imaging as assessed by core laboratory
- Stent migration confirmed by imaging as assessed by core laboratory

Note: Migration excluded dislodgement at the index procedure as may occur with under-sizing of a stent.

The statistical hypothesis was that the primary safety rate through 30 days will not exceed a performance goal established from scientific literature:

H_0: $P \geq PG$

H_A: $P < PG$

where P was the primary safety endpoint at 30 days in the study population and PG was the performance goal of 12.5%.

The review of the literature that provided results on the composite MAE endpoint components suggests an expected rate of 5.6%. The performance goal of 12.5% was set with a margin of 6.9% above the literature derived rate. Exact binomial test was used for the hypothesis testing and the one-sided p-value was reported. The primary safety failure rate was calculated as the number of subjects who had an event within 30 days divided by the number of evaluable subjects who had sufficient follow up (at least 23 days for 30-day visit) without an event plus any subjects who had a MAE within 30 days post-procedure.

The primary safety objective was considered to be met if the upper limit of the 97.5% one-sided confidence interval was below 12.5%. Assuming desired power of at least 92% under difference testing relative to the performance goal at a one-sided alpha of 0.025, the required sample size was 193 subjects using exact binomial test for a single proportion. Accounting for attrition, the sample size was augmented by 3.5% to 200 subjects.

Primary effectiveness endpoint

The primary effectiveness endpoint of the study was Primary Patency at 12 months post index procedure, which required meeting all of the following criteria at 12 months post-procedure:

- Freedom from occlusion of the stented segment of the target lesion, defined as absence of 100% stenosis as measured by venogram (or DUS in the event venogram not available);
- Freedom from restenosis ≥50% of the stented segment of the target lesion, defined as diameter stenosis less than 50% as measured by venogram (or DUS in the event venogram not available);
- Freedom from clinically driven target lesion revascularization, defined as absence of clinically driven reintervention, where clinically driven is defined as the recurrence of symptoms present at baseline or the onset of new symptoms including, but not limited to venous pain, swelling, dermatitis, or ulceration related to the target limb.

The statistical hypothesis was that primary patency through 12 months will exceed a performance goal established from historical literature:

H_0: $\pi \leq PG$

H_A: $\pi > PG$

where π was the primary patency rate at 12 months in the study population and PG was the performance goal of 75%.

Based on an extensive and independent review of the literature, the estimated patency rate was 84% for acute Deep Vein Thrombosis (aDVT) subjects, 96% for NIVL subjects and 80% for PTS subjects. The distribution of patients in the literature on which our PGs were based are 26%, 30% and 44% for aDVT, NIVL, and PTS, respectively. By subtracting a margin of 10% from the weighted average of patency rates of the three patient categories, the value of 75% was taken as the performance goal for the study.

The primary patency rate was calculated as the number of subjects without loss of primary patency divided by the number of subjects having evaluable primary endpoint data for primary patency at 12 months. The primary analysis set was 'included' subjects who were considered evaluable if: (a) the subject experienced at least one clinically-driven target lesion revascularization within 390 days; or (b) the subject had occlusion or restenosis ≥50% of the stented segment of the target lesion confirmed by core laboratory at 12 months visit; or (c) the subject had at least 330 days follow up without an event in the primary effectiveness endpoint. Exact binomial test was used to test the hypothesis and one-sided p-value was reported for primary effectiveness endpoint. The primary effectiveness objective was considered to be met if the lower limit of the 97.5% one-sided confidence interval of the 12-month primary patency rate was above 75%. Assuming desired power of at least 92% under difference testing relative to the performance goal at a one-sided alpha of 0.025, the required sample size was 160 subjects using exact binomial test for a single proportion. Accounting for attrition, the sample size was augmented by 20% to 200 subjects.

The overall power of the study, considering primary effectiveness and primary safety, was at least 84%.

Secondary Endpoints

The following secondary endpoints were evaluated through 12 months (24-month and 36-month evaluations will be performed according to each endpoint definition).

- Device success, defined as successful delivery and deployment of the Abre stent in the target lesion with successful removal of the delivery system.

- Lesion success, defined as venographic evidence of <50% final residual stenosis of the stented segment of the target lesion after post-dilation, when

applicable, and as assessed by core laboratory. If the core laboratory was unable to assess the venographic evidence, site-reported "post-stenting" data were used.

- Procedure success, defined as lesion success without procedure-related MAEs prior to hospital discharge within 30 days.

- Primary assisted patency at 12 months, defined as uninterrupted patency of the stented segment of the target lesion with a secondary intervention, also known as an adjunctive treatment (e.g. balloon venoplasty, subsequent stenting, etc.).

- Secondary patency at 12 months, defined as patency of the stented segment of the target lesion after subsequent intervention for an occlusion.

- TLR through 30 days, 6, 12, 24, and 36 months, defined as any re-intervention of the stented segment of the target lesion.

- MAEs through 6, 12, 24, and 36 months, including all-cause death occurring post-procedure, clinically significant (i.e. symptomatic, confirmed by CT pulmonary angiography) pulmonary embolism, major bleeding complication (post-procedural), stent thrombosis, and stent migration. All MAEs were adjudicated by a CEC, except for stent thrombosis and stent migration, which were confirmed by the core laboratory.

- Delayed stent migration at 12, 24, and 36 months, defined as position change of a venous stent observed with an imaging modality >1 cm from its original location at the conclusion of the index procedure, as determined with regard to a reference anatomic structure.

- Stent fracture at 30 days, 12, 24, and 36 months, defined as fracture or breakage of any portion of the stent determined by X-ray for the first 30 subjects at 30 days and for all subjects (including the first 30 subjects) at 12, 24, and 36 months.

- Change in Venous Insufficiency Epidemiological and Economic Study – Quality of Life/Symptoms (VEINES-QOL/Sym) Scores at 6, 12, 24, and 36 months, compared to baseline.

- Change in Villalta Score at 6, 12, 24, and 36 months, compared to baseline.

- Change in Euro-Qol 5 Dimension (EQ-5D) Quality of life Score at 6, 12, 24, and 36 months, compared to baseline.

- Change in VCSS Score at 6, 12, 24, and 36 months, compared to baseline.

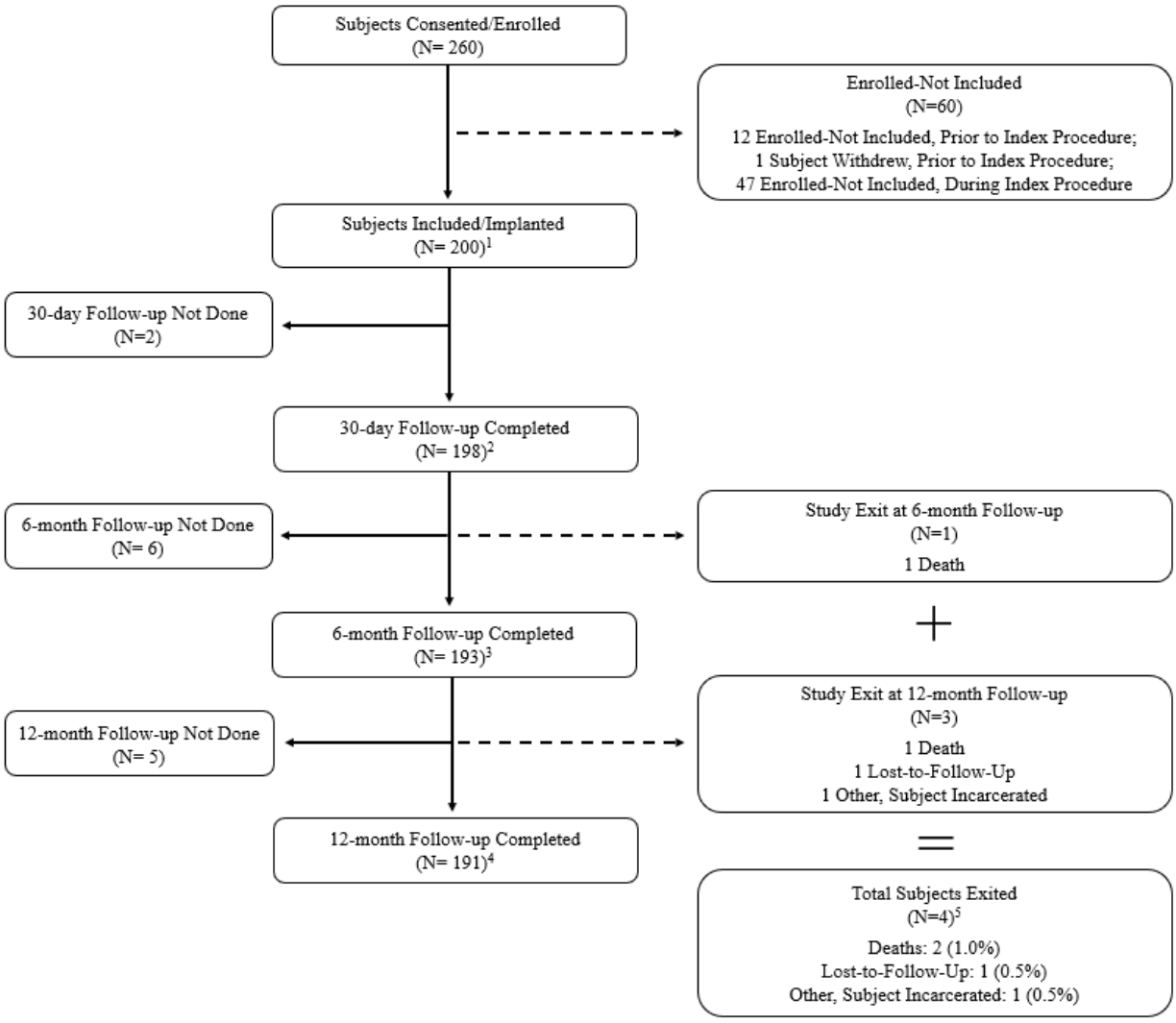
- Major bleeding complications at 30 days, 6, 12, 24, and 36 months.

- Medical resource utilization through 36 months, including length of stay and re-hospitalizations.

B. Accountability of PMA Cohort

A total of 260 subjects signed the ABRE Study informed consent form and were evaluated against inclusion and exclusion criteria for the study. Of these 260 subjects, 200 were implanted with at least one Abre stent. Out of 200 implanted subjects, 191 subjects returned for a 12-month visit, for a follow-up completion rate of 95.5% (191/200). A total of four subjects exited the study prior to completing the 12-month visit. These study exits included two subject deaths (unrelated to the study device or procedure), one subject who was lost to follow-up, and one subject who exited the study due to incarceration. Five subjects missed the 12-month visit.

A detailed breakdown of ABRE subject visit availability per the study follow-up schedule is reported through the 12-month visit and presented in Figure 3. In total, 196 subjects were available for the 12-month visit, and 5 subjects missed the visit for a total of 191 subjects with available 12-month data.



[1]260 consented subjects – 60 enrolled not included subjects = 200 included/implanted subjects
[2]200 included subjects – 2 missed visits = 198 subjects completed 30-day follow-up
[3]200 included subjects – 1 exited subject = 199; 199 included subjects still in study – 6 missed visits = 193 subjects completed 6-month follow-up
[4]199 included subjects still in study – 3 exited subjects = 196 included subjects still in study – 5 missed visits = 191 subjects completed 12-month follow-up
[5]sum of subjects that exited the study as of the January 17, 2020 data cut-off date

Figure 3: Visit Availability

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for the type of study performed in the US and Europe. Site reported subject demographics for all 200 subjects are presented in Table 6 below.

Table 6: Demographics

Parameter	ABRE (N=200 Subjects)
Age at Time of Enrollment (years)	
N	200
Mean ± SD	51.5 ± 15.9
Median	53.0
Min, Max	18, 80
Gender at Birth	
Female	66.5% (133/200)
Male	33.5% (67/200)
BMI (kg/m^2)	
N	200
Mean ± SD	29.5 ± 7.1
Median	28.8
Min, Max	14.9, 53.5
Ethnicity[a]	
Hispanic or Latino	7.0% (14/200)
Not Hispanic or Latino	80.0% (160/200)
Not Available	13.0% (26/200)
Race[a]	
White	78.5% (157/200)
Black or African American	8.5% (17/200)
Asian	2.0% (4/200)
Native Hawaiian/Other Pacific Islander	0.0% (0/200)
American Indian or Alaska Native	0.0% (0/200)
Not Available	11.0% (22/200)
Other	0.0% (0/200)

[a]France does not permit the collection of Race and Ethnicity data from study subjects.
Site-reported data

Site-reported baseline medical history is summarized in Table 7.

Table 7: Baseline Medical History

Parameter	ABRE (N=200 Subjects)
Hypertension	31.0% (62/200)
Hyperlipidemia	28.5% (57/200)
Diabetes Mellitus	10.5% (21/200)
Smoking	
Active	12.0% (24/200)
Previous	30.5% (61/200)
Never	57.5% (115/200)
Cancer (Ongoing or Remission)	11.0% (22/200)
Pulmonary	29.5% (59/200)
Chronic Obstructive Pulmonary Disease	4.5% (9/200)
Pulmonary Embolism	17.0% (34/200)
Pulmonary Hypertension	1.0% (2/200)
Asthma	12.5% (25/200)
Vascular	83.0% (166/200)
Stroke	0.0% (0/200)
TIA	1.0% (2/200)
Peripheral Artery Disease	3.5% (7/200)
Known Family History of DVT	22.0% (44/200)
Previous History of Venous Thromboembolism	52.0% (104/200)
Venous Claudication	30.0% (60/200)
Lymphedema	15.0% (30/200)
Hypercoagulability Syndrome/Thrombophilia	11.5% (23/200)
Cardiac	7.0% (14/200)
Congestive Heart Failure	3.0% (6/200)
Ischemic Heart Disease	3.5% (7/200)
Previous Myocardial Infarction	3.0% (6/200)

Site-reported data

Table 8 presents site-reported target limb baseline clinical characteristics.

Table 8: Target Limb Baseline Clinical Characteristics

Parameter	ABRE (N=200 Subjects)
Target Limb	
Left	92.0% (184/200)
Right	8.0% (16/200)
Presence of lymphedema	14.6% (29/198)
CEAP Classification*	
C0 - No visible or palpable signs of venous disease	0.6% (1/166)
C1 - Telangiectasias or reticular veins	0.6% (1/166)
C2 - Varicose veins	2.4% (4/166)
C3 - Edema	62.0% (103/166)
C4a - Pigmentation or eczema	13.3% (22/166)
C4b - Lipodermatosclerosis or atrophie blanche	6.6% (11/166)
C5 - Healed venous ulcer	6.6% (11/166)
C6 - Active venous ulcer	7.8% (13/166)
Villalta Score	
N	199
Mean ±SD	11.2 ± 5.7
Median	11.0
Min, Max	0.0, 32.0
VCSS Score	
N	199
Mean ±SD	8.8 ± 4.7
Median	8.0
Min, Max	1.0, 27.0

Site-reported data
*PTS and NIVL subjects only; CEAP assessment is not applicable for acute DVT subjects

D. Procedural Characteristics

Site-reported index procedure characteristics are summarized in Table 9. The largest category of subjects (47.5%) were included in the PTS primary indication category, 36.0% were included in the NIVL category, and the remaining 16.5% were categorized as having had an acute DVT.

Table 9: Procedural Characteristics

Parameter	ABRE (N=200 Subjects)
Primary Indication	
Acute DVT	16.5% (33/200)
Post Thrombotic Syndrome	47.5% (95/200)
Non-Thrombotic Iliac Vein Lesion	36.0% (72/200)
Type of Anesthesia Used	
General	81.5% (163/200)
Spinal	0.0% (0/200)
Epidural	0.0% (0/200)
Local	62.0% (124/200)
Access Site	
Common Femoral	23.5% (47/200)
Femoral	49.0% (98/200)
Internal Jugular	3.5% (7/200)
Popliteal	20.0% (40/200)
Superficial Vein	2.5% (5/200)
Other	1.5% (3/200)

Site-reported data

As shown in Table 10, an average of 1.5 stents per subject were implanted during the index procedure. One or more stents were implanted in the common iliac vein in 96% of subjects, in the external iliac vein in 80.5% of subjects, and in the common femoral vein in 44.0% of subjects. The mean total stented length was 134.3 ± 58.0 mm.

Table 10: Venography Core Laboratory Stent Implant Data

Parameter	ABRE (N=200 Subjects)
Subjects with*	
1 Abre Stent Implanted	55.5% (111/200)
2 Abre Stents Implanted	38.5% (77/200)
3 Abre Stents Implanted	5.5% (11/200)
> 3 Abre Stents Implanted	0.5% (1/200)
Number of Abre Stents Implanted per Subject*	
N	200
Mean ±SD	1.5±0.6
Median	1.0
Min, Max	1,4
Stented Vein Location*	
Common Iliac Vein	96.0% (192/200)

Parameter	ABRE (N=200 Subjects)
External Iliac Vein	80.5% (161/200)
Common Femoral Vein	44.0% (88/200)
% Diameter Stenosis	
N	193
Mean ±SD	14.2±8.2
Median	11.7
Min, Max	2,48
Length of Overlap with Cranial Stent (mm) per Stent	
N	95
Mean ±SD	24.6±11.9
Median	23.3
Min, Max	5,68
Total Stented Length (mm)	
N	192
Mean ±SD	134.3±58.0
Median	121.5
Min, Max	49,283

*Site-reported data were used when venography core laboratory-reported data were not available

Table 11 displays the stent usage by diameter and length in the study. A total of 302 Abre stents were implanted in the 200 ABRE Study subjects.

Table 11: Study Stent Usage by Diameter and Length

	Length (mm)						
Diameter(mm)	**40**	**60**	**80**	**100**	**120**	**150**	**Total**
10	0	0	0	0	0	0	**0**
12	NA	6	0	0	2	1	**9**
14	NA	5	12	28	32	33	**110**
16	NA	12	27	29	36	35	**139**
18	NA	5	10	12	7	6	**40**
20	NA	0	0	1	1	2	**4**
Total	**0**	**28**	**49**	**70**	**78**	**77**	**302**

E. Safety and Effectiveness Results

1. Safety Results

For the primary safety endpoint, the MAE rate at 30 days was 2.0% (4/200). The upper bound of the one-sided 97.5% CI was 5.0%, which was significantly lower than the 12.5% performance goal, demonstrating that the primary safety endpoint was met (p-value <0.0001). Table 12 displays the data for each component of the composite MAE rate at 30 days. A total of four subjects were reported having a total of four MAEs within 30 days of the index procedure: three stent thrombosis and one clinically significant pulmonary embolism. No subject deaths, major bleeding complications, or stent migrations occurred during the 30 days following the index procedure.

Table 12: Primary Safety Composite Endpoint – MAE within 30 Days

Parameter	ABRE (N=200 Subjects)	95% Confidence Interval
Primary Safety Composite Endpoint – MAE within 30 Days	2.0% (4/200)	[0.5%, 5.0%]
All-cause Death Occurring Post-Procedure	0.0% (0/200)	[0.0%, 1.8%]
Clinically Significant Pulmonary Embolism	0.5% (1/200)	[0.0%, 2.8%]
Major Bleeding Complication (Procedural)	0.0% (0/200)	[0.0%, 1.8%]
Stent Thrombosis	1.5% (3/200)	[0.3%, 4.3%]
Stent Migration	0.0% (0/200)	[0.0%, 1.8%]

Table 13 displays non-serious adverse events (non-SAEs) occurring from the day of the index procedure through 360 days post index procedure. All data presented herein are site-reported. A total of 276 adverse events (non-SAEs) were reported in 121 subjects. Incidences of Musculoskeletal and connective tissue disorders (18.0%), General disorders and administration site conditions (13.5%), and Injury, poisoning and procedural complications (13.5%) were the most commonly reported events.

Table 13: Number of Subjects with One or More Adverse Events (Non - SAEs) through 360 Days by MedDRA System-Organ Class and Preferred Term

Adverse Event	Included Subjects (N=200 Subjects)
Subjects with One or More Adverse Events	**60.5% (121/200)**
System-organ class/preferred term	
Blood And Lymphatic System Disorders	**1.5% (3/200)**
Anaemia	1.0% (2/200)
Coagulopathy	0.5% (1/200)
Leukopenia	0.5% (1/200)
Cardiac Disorders	**1.5% (3/200)**

Adverse Event	Included Subjects (N=200 Subjects)
Angina Pectoris	0.5% (1/200)
Atrial Fibrillation	0.5% (1/200)
Palpitations	0.5% (1/200)
Ear And Labyrinth Disorders	**1.0% (2/200)**
Vertigo	1.0% (2/200)
Endocrine Disorders	**2.0% (4/200)**
Hyperthyroidism	0.5% (1/200)
Hypothyroidism	1.5% (3/200)
Eye Disorders	**1.5% (3/200)**
Chalazion	0.5% (1/200)
Conjunctival Haemorrhage	0.5% (1/200)
Visual Impairment	0.5% (1/200)
Gastrointestinal Disorders	**6.5% (13/200)**
Abdominal Pain	2.0% (4/200)
Abdominal Pain Upper	1.0% (2/200)
Diarrhoea	1.0% (2/200)
Gastritis	1.0% (2/200)
Gingival Bleeding	0.5% (1/200)
Haematochezia	1.0% (2/200)
Ileus	0.5% (1/200)
Nausea	1.0% (2/200)
Rectal Haemorrhage	1.0% (2/200)
General Disorders And Administration Site Conditions	**13.5% (27/200)**
Adverse Drug Reaction	0.5% (1/200)
Chest Pain	0.5% (1/200)
Crepitations	0.5% (1/200)
Cyst	0.5% (1/200)
Drug Intolerance	0.5% (1/200)
Fatigue	0.5% (1/200)
Injection Site Haemorrhage	0.5% (1/200)
Medical Device Site Pain	0.5% (1/200)
Nodule	0.5% (1/200)
Non-Cardiac Chest Pain	1.0% (2/200)
Pain	0.5% (1/200)
Peripheral Swelling	0.5% (1/200)
Pyrexia	0.5% (1/200)
Swelling	0.5% (1/200)
Vascular Stent Stenosis	3.0% (6/200)
Vascular Stent Thrombosis	3.5% (7/200)
Vessel Puncture Site Haematoma	0.5% (1/200)

Adverse Event	Included Subjects (N=200 Subjects)
Vessel Puncture Site Haemorrhage	0.5% (1/200)
Hepatobiliary Disorders	**0.5% (1/200)**
Cholelithiasis	0.5% (1/200)
Immune System Disorders	**0.5% (1/200)**
Contrast Media Reaction	0.5% (1/200)
Infections And Infestations	**11.5% (23/200)**
Abscess Limb	0.5% (1/200)
Bacterial Tracheitis	0.5% (1/200)
Bronchitis	2.0% (4/200)
Cellulitis	1.0% (2/200)
Clostridium Difficile Infection	0.5% (1/200)
Gastroenteritis	0.5% (1/200)
Infectious Mononucleosis	0.5% (1/200)
Influenza	1.5% (3/200)
Lower Respiratory Tract Infection	1.5% (3/200)
Nasopharyngitis	1.0% (2/200)
Peritonsillar Abscess	0.5% (1/200)
Pneumonia Viral	0.5% (1/200)
Sialoadenitis	0.5% (1/200)
Sinusitis	0.5% (1/200)
Tonsillitis	0.5% (1/200)
Upper Respiratory Tract Infection	0.5% (1/200)
Urinary Tract Infection	1.0% (2/200)
Viral Upper Respiratory Tract Infection	0.5% (1/200)
Injury, Poisoning And Procedural Complications	**13.5% (27/200)**
Contusion	3.5% (7/200)
Device Difficult To Use	0.5% (1/200)
Epicondylitis	0.5% (1/200)
Fall	0.5% (1/200)
Foot Fracture	1.5% (3/200)
Joint Dislocation	0.5% (1/200)
Ligament Sprain	0.5% (1/200)
Limb Injury	1.0% (2/200)
Meniscus Injury	0.5% (1/200)
Peripheral Nerve Injury	0.5% (1/200)
Post Procedural Discharge	0.5% (1/200)
Post Procedural Haematuria	0.5% (1/200)
Post-Traumatic Pain	0.5% (1/200)
Procedural Pain	0.5% (1/200)
Skin Laceration	1.5% (3/200)

Adverse Event	Included Subjects (N=200 Subjects)
Vascular Access Site Bruising	0.5% (1/200)
Vascular Access Site Complication	0.5% (1/200)
Vascular Access Site Haematoma	1.0% (2/200)
Investigations	**2.5% (5/200)**
Blood Urine Present	0.5% (1/200)
Cardiolipin Antibody Positive	0.5% (1/200)
Haemoglobin Decreased	1.0% (2/200)
Oesophagogastroduodenoscopy	0.5% (1/200)
Metabolism And Nutrition Disorders	**1.5% (3/200)**
Decreased Appetite	0.5% (1/200)
Hypernatraemia	0.5% (1/200)
Hypokalaemia	0.5% (1/200)
Hypovolaemia	0.5% (1/200)
Iron Deficiency	0.5% (1/200)
Vitamin B12 Deficiency	0.5% (1/200)
Musculoskeletal And Connective Tissue Disorders	**18.0% (36/200)**
Arthralgia	2.5% (5/200)
Arthritis	1.0% (2/200)
Back Pain	3.5% (7/200)
Bursitis	0.5% (1/200)
Groin Pain	1.0% (2/200)
Intervertebral Disc Degeneration	0.5% (1/200)
Limb Discomfort	0.5% (1/200)
Muscle Tightness	0.5% (1/200)
Musculoskeletal Chest Pain	0.5% (1/200)
Musculoskeletal Pain	1.0% (2/200)
Pain In Extremity	6.5% (13/200)
Patellofemoral Pain Syndrome	0.5% (1/200)
Rheumatoid Arthritis	0.5% (1/200)
Synovial Cyst	0.5% (1/200)
Tendonitis	0.5% (1/200)
Tenosynovitis	0.5% (1/200)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	**1.0% (2/200)**
Basal Cell Carcinoma	0.5% (1/200)
Lipoma	0.5% (1/200)
Nervous System Disorders	**7.5% (15/200)**
Carpal Tunnel Syndrome	0.5% (1/200)
Coordination Abnormal	0.5% (1/200)
Dizziness	0.5% (1/200)

Adverse Event	Included Subjects (N=200 Subjects)
Headache	1.0% (2/200)
Hypoaesthesia	1.5% (3/200)
Migraine	0.5% (1/200)
Neuralgia	1.0% (2/200)
Neuropathy Peripheral	0.5% (1/200)
Paraesthesia	0.5% (1/200)
Sciatica	1.0% (2/200)
Spinal Subdural Haematoma	0.5% (1/200)
Psychiatric Disorders	**1.0% (2/200)**
Depression	0.5% (1/200)
Stress	0.5% (1/200)
Renal And Urinary Disorders	**3.5% (7/200)**
Acute Kidney Injury	1.0% (2/200)
Dysuria	0.5% (1/200)
Haematuria	2.0% (4/200)
Haemoglobinuria	0.5% (1/200)
Reproductive System And Breast Disorders	**3.5% (7/200)**
Adenomyosis	0.5% (1/200)
Breast Mass	1.0% (2/200)
Breast Pain	0.5% (1/200)
Pelvic Pain	0.5% (1/200)
Postmenopausal Haemorrhage	0.5% (1/200)
Prostatitis	0.5% (1/200)
Respiratory, Thoracic And Mediastinal Disorders	**6.0% (12/200)**
Asthma	1.0% (2/200)
Bronchospasm	0.5% (1/200)
Cough	0.5% (1/200)
Dyspnoea	1.0% (2/200)
Dyspnoea Exertional	0.5% (1/200)
Epistaxis	2.0% (4/200)
Lung Consolidation	0.5% (1/200)
Skin And Subcutaneous Tissue Disorders	**7.0% (14/200)**
Dermatitis Allergic	1.0% (2/200)
Dermatitis Contact	0.5% (1/200)
Eczema	0.5% (1/200)
Neuropathic Ulcer	0.5% (1/200)
Psoriasis	0.5% (1/200)
Rash	1.0% (2/200)
Skin Ulcer	3.5% (7/200)
Vascular Disorders	**13.0% (26/200)**

Adverse Event	Included Subjects (N=200 Subjects)
Deep Vein Thrombosis	1.5% (3/200)
Haematoma	1.0% (2/200)
Hypertension	1.5% (3/200)
Hypotension	0.5% (1/200)
Lymphocele	0.5% (1/200)
Lymphoedema	4.5% (9/200)
Peripheral Venous Disease	1.5% (3/200)
Post Thrombotic Syndrome	0.5% (1/200)
Subclavian Artery Occlusion	0.5% (1/200)
Thrombophlebitis	0.5% (1/200)
Thrombophlebitis Superficial	1.0% (2/200)
Varicose Vein	1.5% (3/200)
Venous Hypertension	1.5% (3/200)
Total Adverse Events	**276**

MedDRA version 22.0
Site reported data.

Table 14 displays serious adverse events (SAEs) that occurred from the day of the index procedure through 360 days post index procedure. All data presented herein are site-reported. A total of 104 SAEs were reported in 59 subjects. In total, 29.5% of subjects experienced one or more SAEs. Incidences of General disorders and administration site conditions (12.5%) and Vascular disorders (6.0%) were the most commonly reported events.

Table 14: Number of Subjects with One or More Serious Adverse Events (SAEs) through 360 Days by MedDRA System-Organ Class and Preferred Term

Serious Adverse Event	Included Subjects (N=200 Subjects)
Subjects with One or More Serious Adverse Events	**29.5% (59/200)**
System-organ class/preferred term	
Blood And Lymphatic System Disorders	**1.0% (2/200)**
Anaemia	1.0% (2/200)
Cardiac Disorders	**3.0% (6/200)**
Acute Left Ventricular Failure	0.5% (1/200)
Acute Myocardial Infarction	0.5% (1/200)
Atrial Fibrillation	2.0% (4/200)
Cardiac Failure Congestive	0.5% (1/200)
Supraventricular Tachycardia	0.5% (1/200)

Serious Adverse Event	Included Subjects (N=200 Subjects)
Gastrointestinal Disorders	**2.5% (5/200)**
Abdominal Hernia	1.0% (2/200)
Abdominal Wall Haematoma	0.5% (1/200)
Anal Fissure	0.5% (1/200)
Haemorrhoids	0.5% (1/200)
Retroperitoneal Haematoma	0.5% (1/200)
Small Intestinal Obstruction	0.5% (1/200)
General Disorders And Administration Site Conditions	**12.5% (25/200)**
Fatigue	0.5% (1/200)
Multiple Organ Dysfunction Syndrome	0.5% (1/200)
Peripheral Swelling	0.5% (1/200)
Vascular Stent Stenosis	4.0% (8/200)
Vascular Stent Thrombosis	9.0% (18/200)
Infections And Infestations	**2.5% (5/200)**
Intervertebral Discitis	0.5% (1/200)
Pneumonia	1.5% (3/200)
Pyelonephritis	0.5% (1/200)
Septic Shock	0.5% (1/200)
Injury, Poisoning And Procedural Complications	**3.0% (6/200)**
Meniscus Injury	1.0% (2/200)
Spinal Compression Fracture	0.5% (1/200)
Tendon Rupture	0.5% (1/200)
Vascular Access Site Haematoma	1.0% (2/200)
Investigations	**0.5% (1/200)**
Haemoglobin Decreased	0.5% (1/200)
Musculoskeletal And Connective Tissue Disorders	**3.5% (7/200)**
Arthralgia	0.5% (1/200)
Back Pain	1.0% (2/200)
Intervertebral Disc Protrusion	0.5% (1/200)
Osteoarthritis	1.5% (3/200)
Nervous System Disorders	**2.0% (4/200)**
Cerebrovascular Accident	0.5% (1/200)
Intracranial Aneurysm	0.5% (1/200)
Migraine	0.5% (1/200)
Nerve Compression	0.5% (1/200)

Serious Adverse Event	Included Subjects (N=200 Subjects)
Renal And Urinary Disorders	**1.5% (3/200)**
Acute Kidney Injury	1.0% (2/200)
Haematuria	0.5% (1/200)
Respiratory, Thoracic And Mediastinal Disorders	**4.0% (8/200)**
Bronchiectasis	0.5% (1/200)
Dyspnoea Exertional	1.0% (2/200)
Epistaxis	0.5% (1/200)
Pleural Effusion	1.0% (2/200)
Pulmonary Embolism	0.5% (1/200)
Respiratory Failure	0.5% (1/200)
Skin And Subcutaneous Tissue Disorders	**1.5% (3/200)**
Skin Ulcer	1.0% (2/200)
Stasis Dermatitis	0.5% (1/200)
Vascular Disorders	**6.0% (12/200)**
Deep Vein Thrombosis	2.0% (4/200)
Lymphoedema	1.0% (2/200)
Peripheral Artery Stenosis	0.5% (1/200)
Peripheral Venous Disease	0.5% (1/200)
Varicose Vein	1.5% (3/200)
Vena Cava Thrombosis	0.5% (1/200)
Venous Haemorrhage	0.5% (1/200)
Total Serious Adverse Events	**104**

MedDRA version 22.0
Site-reported data.

2. Effectiveness Results

The primary patency rate at 12 months was 88.0% (162/184). For the primary effectiveness endpoint, 184 evaluable subjects were included in the primary analysis and 16 subjects were excluded per the SAP due to the following: four subjects did not have sufficient clinical follow-up of at least 330 days (two deaths and two study exits), four subjects missed the 12-month visit. The remaining eight subjects were censored from the analysis due to having a CEC-adjudicated non-clinically driven target lesion revascularization (TLR). The lower limit of the 97.5% one-sided confidence interval (CI) was 82.5%, which was significantly higher than the performance goal of 75%, demonstrating that the primary effectiveness endpoint was met (p-value <0.0001). Table 15 displays the 12-month

primary patency rate of 88.0%, as well as the individual components of primary patency. Among the subjects evaluable for primary patency, the freedom from occlusion rate at 12 months was 99.5%, the freedom from restenosis rate at 12 months was 92.9%, and the freedom from clinically driven TLR rate through 12 months was 92.4%.

Table 15: Primary Effectiveness Endpoint – Primary Patency at 12 months

Parameter	ABRE (N=200 Subjects)	95% Confidence Interval
Primary Effectiveness Endpoint – Primary Patency at 12 Months	88.0% (162/184)	[82.5%, 92.4%]
Freedom from Occlusion of the Stented Segment of the Target Lesion	99.5% (183/184)	[97.0%, 100.0%]
Freedom from Restenosis (≥50%) of the Stented Segment	92.9% (171/184)	[88.2%, 96.2%]
Freedom from Clinically Driven Target Lesion Revascularization	92.4% (170/184)	[87.6%, 95.8%]

3. Secondary Endpoint Results

Table 16 shows the results for the acute and late success secondary endpoints.

Table 16: Acute and Late Success Secondary Endpoints

Parameter	ABRE (N=200 Subjects) (N=302 Devices)
Acute Success	
Device Success	100.0% (302/302)
Lesion Success	100.0% (200/200)
Procedure Success	99.0% (198/200)
Late Success	
Primary Assisted Patency at 12 months	91.8% (169/184)
Secondary Patency at 12 months	92.9% (171/184)

Cumulative outcomes for the safety-related secondary endpoints through 12 months are shown below in Table 17. TLR was defined as any reintervention of the stented segment of the target lesion. The TLR rate, which includes both clinically driven and non-clinically driven TLRs, was 11.2% at 12 months. The MAE rate was 6.1% within 360 days. The individual components of this composite MAE rate are also shown. There were two deaths reported in the study, the first occurred 66 days from the index procedure and the second occurred 252 days from the index procedure. Both deaths were adjudicated by the CEC as not related to the procedure

and not related to the study device.

No stent fractures or delayed stent migrations were reported through 12 months. No procedure-related major bleeding complications were reported.

Table 17: Cumulative Complications within 12 Months

Parameter	ABRE (N=200 Subjects)
TLR within 360 Days[†]	11.2% (22/196)
MAE within 360 Days[†]	6.1% (12/197)
All-cause Death Occurring Post-procedure	1.0% (2/197)
Clinically Significant Pulmonary Embolism	0.5% (1/195)
Major Bleeding Complication (Post-procedural)	0.5% (1/195)
Stent Thrombosis	4.1% (8/195)
Stent Migration	0.0% (0/195)
Stent Fracture through 12 Months[††]	0.0% (0/180)
Delayed Stent Migration through 12 Months[††]	0.0% (0/181)
Major Bleeding Related to Index Procedure within 360 Days[†]	0.0% (0/195)

[†]Safety endpoints (TLR, MAE, and Major Bleeding) included subjects with an event or a minimum number of follow-up days per timepoint.
[††]Stent Fracture and Delayed Stent Migration within 12 months included subjects who had scheduled visit-based evaluable imaging and unscheduled imaging up to day 420.

Clinical endpoints at 12 months evaluated changes in functional assessments (VCSS and Villalta) and quality of life (EQ-5D Index and VEINES-QoL) compared to baseline. Trends toward improvement were noted from baseline to 12 months for all four measures, as shown in Table 18.

Table 18: Quality of Life and Venous Functional Assessment Data

Assessment	Baseline Mean ± SE (n)	6 Months Mean ± SE (n)	12 Months Mean ± SE (n)
VEINES-QoL	49.9 ± 1.8 (200)	72.1 ± 1.8 (192)	72.8 ± 1.8 (192)
EQ-5D Index	0.66 ± 0.02 (200)	0.81 ± 0.01 (192)	0.80 ± 0.02 (192)
Villalta score	11.2 ± 0.4 (199)	4.7 ± 0.3 (191)	4.2 ± 0.4 (192)
VCSS score	8.8 ± 0.3 (199)	4.7 ± 0.3 (191)	4.3 ± 0.3 (192)

4. Subgroup Analyses

The primary effectiveness and safety results were analyzed by different subgroups including gender, geographic region, and patient population. The study was not specifically powered for these subgroup analyses.

Primary patency at 12 months was lower in female subjects compared to male subjects (84.6% vs. 95.1%, p-value=0.052). US subjects had a higher primary patency rate compared to OUS subjects (91.7% vs. 81.3%, p-value=0.055). This can be explained by the higher proportion of PTS subjects enrolled at OUS sites (70.8%) compared to US sites (34.4%). Among the three patient populations, aDVT, PTS and NIVL, the primary patency rate at 12 months was highest in NIVL subjects (98.6%) and lowest in PTS subjects (79.8%). This is consistent with what has been reported in the literature.

No significant differences were noted for primary safety based on gender, geographic region or patient population.

5. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

F. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 102 investigators, of which one was a full-time or part-time employee of the sponsor, and seven had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: Seven
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the

information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The *in vitro* testing conducted on the Abre Venous Self-expanding Stent System demonstrated that the performance characteristics met the defined product specifications. The test results obtained from the sterilization testing demonstrated that the product can be adequately sterilized and is acceptable for clinical use. The shelf life testing has established acceptable performance for a labeled shelf life up to 3 years.

The prospective, interventional, non-randomized, single-arm, multi-center, global ABRE Study was designed to evaluate the Abre Venous Self-expanding Stent System for the treatment of symptomatic iliofemoral venous outflow obstruction. The primary effectiveness endpoint was 12-month primary patency, defined as freedom from clinically driven revascularization, occlusion and stenosis. The primary patency rate at 12 months was 88.0% (162/184). The lower limit of the 97.5% one-sided confidence interval (CI) was 82.5%, which was significantly higher than the performance goal of 75%, demonstrating that the primary effectiveness endpoint was met (p-value <0.0001). In addition, patients demonstrated clinically meaningful improvement in quality of life and functional assessments, including VEINES-QoL, EQ-5D index, Villalta, and VCSS.

B. Safety Conclusions

The biocompatibility and *in vivo* animal testing demonstrated that the acute and chronic *in vivo* performance characteristics of the Abre Venous Self-expanding Stent System support a reasonable assurance of safety for the intended clinical use.

The ABRE Study met the primary safety endpoint of composite MAEs at 30 days post-procedure, with potential MAEs including the following:

- all-cause death occurring post-procedure,
- clinically significant pulmonary embolism (i.e., symptomatic, confirmed by CT pulmonary angiography),
- major bleeding complication (procedural),
- stent thrombosis, and
- stent migration.

The primary safety rate at 30 days was 2.0% (4/200). These included one clinically significant pulmonary embolism and three stent thromboses. The upper bound of the one-sided 97.5% CI was 5.0%, which was lower than the 12.5% performance goal, demonstrating that the primary safety endpoint was met (p-value <0.0001). Additionally, no subject deaths, major bleeding complications, or stent migrations occurred during the 30 days following the index procedure. There were also no

delayed stent migrations or stent fractures reported in the study through 12-month follow-up.

C. Benefit-Risk Determination

The probable benefits and risks of the device are also based on data collected in the ABRE Study conducted to support PMA approval as described above. The probable benefit of using the Abre Venous Self-expanding Stent System to treat symptomatic iliofemoral venous outflow obstruction includes restoration of blood flow to improve quality of life and reduce venous disease related symptoms.

The probable risks of the device are also based on data collected in the ABRE Study as described above. The frequency and types of the adverse events reported through the pivotal clinical study are in alignment with those that might be expected in the studied patient population and therapeutic area.

1. Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for treatment of symptomatic iliofemoral venous outflow obstruction, the probable benefits for using the Abre Venous Self-expanding Stent System outweigh the probable risks.

D. Overall Conclusions

The non-clinical and clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The ABRE Study met its primary safety and effectiveness success criteria by having a MAE rate at 30 days lower than the primary safety performance goal and by exceeding the 12-month primary patency performance goal, respectively. The non-clinical and clinical data, including the results of the ABRE Study, demonstrate that the Abre Venous Self-expanding Stent System is safe and effective in the treatment of symptomatic iliofemoral venous obstruction when used in accordance with the labeling and Instructions for Use.

XIII. CDRH DECISION

CDRH issued an approval order on October 21, 2020.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.