Covera™ Vascular Covered Stent

Instructions for Use

BARD | PERIPHERAL VASCULAR

B05872 Rev.6/04-22

DEVICE DESCRIPTION

IMPLANT

The Covera™ Vascular Covered Stent is a flexible, self-expanding endoprosthesis comprised of expanded polytetrafluoroethylene (ePTFE) encapsulating a nitinol (nickel-titanium) stent framework. The inner lumen of the covered stent (blood contacting surface) is carbon impregnated.

The Covera™ Vascular Covered Stent is available in a variety of diameters and lengths and in straight (Figure 1) and flared (Figure 2) configurations. The distal (outflow) end of the flared configuration device is approximately 3 mm larger in diameter than the body and begins approximately 15 mm from the distal end of the device.

Figure 1: Straight Configuration

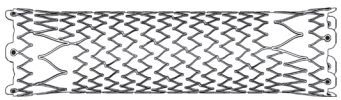
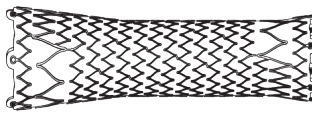


Figure 2: Flared Configuration



Straight device configurations are intended for use in anatomies where the diameter of the outflow vessel is equal to or smaller than the diameter of the inflow vessel. Flared device configurations are intended for use in anatomies where the diameter of the outflow vessel segment is larger than the inflow segment.

COVERED STENT SIZE SELECTION

Special care must be taken to ensure that an appropriately sized device is selected. In the case of a diameter difference between the inflow and the outflow end, utilize the following as the reference vessel depending on the type of access. For an AV graft access, utilize the graft diameter and for an AV fistula access, utilize the inflow vein diameter.

Table 1: Covered Stent Diameter Selection

Covered Stent Diameter	Recommended Oversizing	Reference Vessel or Graft Diameter
6 mm	0.5 mm – 1.5 mm	4.5 mm – 5.5 mm
7 mm	0.5 mm – 1.5 mm	5.5 mm – 6.5 mm
8 mm	1 mm – 2 mm	6 mm – 7 mm
9 mm	1 mm – 2 mm	7 mm – 8 mm
10 mm	1 mm – 2 mm	8 mm – 9 mm

Note: Covered stent length change ranges from -2% to 3% depending upon covered stent diameter selection. Change in length is a mathematical calculation between the undeployed mounted covered stent inside the delivery system and the expanded labeled-diameter condition. A negative value describes covered stent shortening whereas a positive value describes covered stent elongation.

Covered Stent Length

Ensure the selected covered stent length covers the entire lesion and both ends of the implant extend at least 5 mm into the non-diseased segment of the vessel. For covered stent placements in the proximal cephalic arch select the length so that the ostial lesion is fully covered and that the proximal covered stent end does not compromise the flow in the axillary / subclavian vein. Ensure that the covered stent end extends at least 10 mm beyond the arch curvature into the straight distal cephalic vein segment. For covered stent placement in the juxta-anastomotic location of an AV fistula, careful device selection is needed to ensure that the device does not extend into the inflow artery.

X-RAY MARKERS

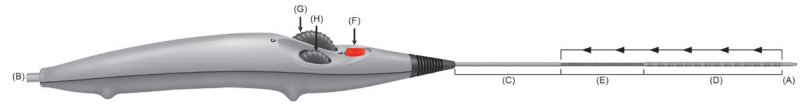
Radiopaque ePTFE encapsulated tantalum markers are evenly distributed around the circumference of the proximal and distal ends of the covered stent.

DELIVERY SYSTEM

The delivery system is illustrated in Figure 3. The inner catheter (not visible to the operator) contains the guidewire lumen. An atraumatic tip (A) is affixed to the distal end of the inner catheter which terminates at the female Luer connector (B) at the proximal end of the handle. A proximal white stability sheath (C) is connected to the distal end of the handle and remains stationary throughout the deployment process.

The distal catheter assembly (30 cm in length) consists of two segments. The transparent covered stent delivery sheath (D), housing the compressed covered stent (implant) and a darker brown, smaller diameter extension catheter (E). During covered stent deployment, the entire distal catheter assembly retracts towards the handle while the dark catheter segment is drawn inside the white stability sheath until the covered stent is fully deployed.
Retraction of the distal catheter and deployment of the covered stent is initiated by rotating the large wheel (G) on the handle. The large deployment wheel is used for the initiation of deployment and a slower deployment rate whereas the small deployment wheel (H) may be used for faster deployment after initiation.

Figure 3: Itemized Drawing of the Covera™ Vascular Covered Stent Delivery System



A red safety lock (F) on the handle prevents premature release of the covered stent. Prior to covered stent deployment, the safety lock must be retracted from the locked position into the unlocked position (Figure 4).

Figure 4: Handle Top View

1 = Red Safety Lock (F)
2 = Large Deployment Wheel for initial and slow deployment (G)
3 = Small Deployment Wheel for faster deployment (H)

Legend for Figures 3 & 4

Reference	Corresponding Information
A	Delivery System Tip
B	Female Luer Port
C	Proximal Stability Sheath (white, stationary)
D	Distal Catheter Sheath Segment (transparent, retracts during deployment) housing the Compressed Covered Stent
E	Distal Catheter Sheath Segment (dark brown, retracts during deployment)
F	Red Safety Lock
G	Large Deployment Wheel (initial and slow deployment)
H	Small Deployment Wheel (fast deployment)

The Covera™ Vascular Covered Stent device is an over-the-wire delivery system. The delivery system is compatible with 0.035 inch guidewires and 8F or 9F introducer sheaths. The delivery system is available in working lengths of 80 cm and 120 cm.

INDICATION FOR USE

The Covera™ Vascular Covered Stent is indicated for use in hemodialysis patients for the treatment of stenoses in the venous outflow of an arterio-venous (AV) fistula and at the venous anastomosis of an ePTFE or other synthetic AV graft.

CONTRAINDICATIONS

There are no known contraindications for the Covera™ Vascular Covered Stent.

WARNINGS

- **This device should be used only by physicians who are familiar with the complications, side effects, and hazards commonly associated with dialysis access shunt revisions and endovascular procedures.**
- **DO NOT expose the covered stent to temperatures higher than 500 °F (260 °C). ePTFE decomposes at elevated temperatures, producing highly toxic decomposition byproducts.**
- **DO NOT use the device if packaging / pouch is damaged.**
- **The Covera™ Vascular Covered Stent device is supplied STERILE and is intended for SINGLE USE ONLY. DO NOT RESTERILIZE AND/OR REUSE this device.**
- **DO NOT use in patients with uncorrectable coagulation disorders.**
- **DO NOT use in patients with bacteremia or septicaemia and/or evidence of fistula or graft infection.**
- **DO NOT use in patients that cannot be adequately premedicated and have a known allergy or sensitivity to contrast media.**
- **DO NOT use in patients with known hypersensitivity to nickel-titanium or tantalum.**
- **DO NOT use in an immature fistula or in patients whose AV Access grafts have been implanted less than 30 days.**
- **DO NOT use the device in patients where full expansion of an appropriately sized PTA balloon catheter could not be achieved during pre-dilation with an angioplasty balloon.**
- **Placing a covered stent across a vessel side branch may impede blood flow and hinder or prevent future procedures.**
- **Covered stent placement beyond the ostium of the cephalic vein into the axillary/subclavian vein may hinder or prevent future access.**
- **DO NOT place a flared covered stent with the flared end in a straight vessel segment since this may lead to flow turbulences. The flared end is not intended to provide additional device fixation.**

PRECAUTIONS

- **Prior to covered stent implantation refer to the sizing table (Table 1) and read the Instructions for Use. Careful attention should be paid to ensure the device is appropriately sized to the vessel diameter, taking into account any change in the vessel diameter that may have resulted from previous interventions. For an AV graft access, utilize the graft diameter as the reference vessel and for an AV fistula access, utilize the inflow vein diameter as the reference vessel.**
- **The appropriate length device should be selected so that the stent graft extends beyond the stenosis into at least 5 mm of the non-diseased fistula or graft towards the arterial inflow and into the non-diseased vein approximately 5 mm beyond the stenosis.**
- **The delivery system is not intended for any use other than covered stent deployment.**
- **The covered stent (implant) cannot be repositioned after total or partial deployment.**
- **Once partially or fully deployed, the covered stent cannot be retracted or remounted onto the delivery system. Device removal after deployment can only be done with a surgical approach.**
- **If unusual resistance is met during covered stent system introduction, the system should be removed and another covered stent system should be used.**
- **DO NOT introduce, manipulate or remove the delivery system without an appropriately sized guidewire in place and without fluoroscopic guidance.**
- **DO NOT kink or use a kinked delivery system.**
- **During covered stent release DO NOT hold the 30 cm long distal catheter assembly segment as it must be free to move and slide into the white stability sheath.**
- **Careful attention by the operator is warranted to mitigate the potential for distal migration of the covered stent during deployment.**
- **Post dilation of the covered stent must be performed using an appropriately sized PTA balloon catheter to avoid damage to the covered stent. The covered stent cannot be post dilated beyond its labelled diameter. The flared distal end does not require post dilation.**
- **The effect of placing the device across an aneurysm or a pseudo-aneurysm has not been evaluated.**
- **The effect of using the device in central veins has not been evaluated.**
- **The effect of placing the device across a previously placed bare metal stent has not been evaluated.**
- **The effect of placing the device across the antecubital fossa has not been evaluated.**
- **The effect of using the device in pediatrics has not been evaluated.**
- **The effect of using the device across the anastomosis of an AV fistula has not been evaluated.**
- **Vessel angulation was not measured as part of the clinical study, as such limitations in covered stent angulation are unknown.**
- **DO NOT cannulate the covered stent. Notify the patient that the covered stent should not be directly cannulated for hemodialysis and that applying pressure to the implant area should be avoided.**
- **The device has not been tested for use in an overlapped condition with a bare metal stent or covered stent.**
- **Higher deployment force may be encountered with longer length covered stents.**
- **The device has not been tested for tracking and deployment around an AV loop graft.**
- **Serious complications, such as migration to the heart or lungs, may occur post-discharge when covered stents have not been appropriately sized.**
- **Stent graft dislodgement may occur during removal of the delivery system; therefore, careful attention should be paid during this portion of the procedure to prevent such occurrences.**

MAGNETIC RESONANCE IMAGING (MRI) COMPATIBILITY

Non-clinical testing has demonstrated that the Covera™ Vascular Covered Stent is MR Conditional for placement in the vessels of the arm for all clinically relevant lengths. Based upon the preclinical testing, patients with the Covera™ Vascular Covered Stent can be scanned safely, immediately after placement of this implant, under the following conditions:

- Static magnetic field of 1.5 Tesla or 3.0 Tesla.
- Spatial gradient field of 3000 Gauss/cm or less.
- Maximum whole-body-averaged specific absorption rate (SAR) of 1 W/kg for 15 minutes of scanning.

3.0 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 6 x 100 mm Covera™ Vascular Covered Stent was determined to produce a potential worst-case temperature rise of 2.9 °C at a whole body SAR of 1 W/kg for 15 minutes of MR scanning in a 3.0 Tesla whole body MR system. Cooling due to blood flow inside the covered stent and perfusion in the vascular bed surrounding the covered stent was included in the assessment of in-vivo temperature rise.

1.5 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 6 x 100 mm Covera™ Vascular Covered Stent was determined to produce a potential worst-case temperature rise of 2.7 °C at the a whole body SAR of 1 W/kg for 15 minutes of MR scanning in a 1.5 Tesla whole body MR system. Cooling due to blood flow inside the covered stent and perfusion in the vascular bed surrounding the covered stent was included in the assessment of in-vivo temperature rise.

Image Artifact

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the covered stent. Artifact tests were performed according to ASTM F2119-07. Maximum artifact extended 5.5 mm beyond the covered stent for the spin echo sequence and 5.5 mm for the gradient echo sequence. The lumen was obscured.

Additional Information

Good clinical MR practice should be followed, including placement of padding between the bore wall and the patient and avoiding contact between the hands and the body.

The Covera™ Vascular Covered Stent has not been evaluated in MRI systems with field strengths other than 1.5 or 3.0 Tesla. The heating effect in the MRI environment for fractured covered stents is not known. The presence of other implants or the health state of the patient may require reduction of the MRI limits listed above.

POTENTIAL COMPLICATIONS AND ADVERSE EVENTS

Complications and Adverse Events associated with the use of the Covera™ Vascular Covered Stent may include the usual complications associated with endovascular stent and covered stent placement and dialysis shunt revisions. In the clinical study of treatment of stenoses in the venous outflow of an arteriovenous fistula, development of new access circuit lesions has been reported at a higher rate for Covera™ Vascular Covered Stent treated subjects compared to PTA treated subjects. Sixty (60) subjects treated with Covera™ Vascular Covered Stent required reinterventions involving new lesions compared to 40 subjects who were treated with PTA alone. See Table 43 below for additional details.

Potential complications may include, but are not limited to:
New lesions in the access circuit requiring reintervention, Thrombotic occlusion, restenosis of the target lesion requiring reintervention, pseudoaneurysm, vessel rupture, dissection, extravasation, perforation, pain, infection, hemorrhage, hematoma, arm or hand edema, steal syndrome, congestive heart failure, cerebrovascular accident, allergic reaction, rash, reaction to contrast, fever, sepsis, prolonged bleeding, ventricular fibrillation, face or neck edema, bleeding at access site, numbness, venous spasm, hemoptysis and death.

Covered stent specific events that could be associated with clinical complications include:
Misplacement, migration, embolism, fracture, compression, kinking and insufficient covered stent expansion.

Delivery System specific events that could be associated with clinical complications include:
Bond joint failures, detachment of parts, incompatibility with accessory devices, premature deployment, inaccurate deployment, failure to deploy, high deployment forces, delivery system kinking, poor visibility under fluoroscopy, inability to track to target location and blood leakage from delivery system.

HOW SUPPLIED
The Covera™ Vascular Covered Stent is supplied sterile (by ethylene oxide gas). For single use only.

STORAGE
Store in a cool, dry place. Keep away from sunlight. **DO NOT** use the device after the "Use By" date specified on the label.

DISPOSAL INSTRUCTIONS
After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations.

CLINICAL USE INFORMATION
- Read all instructions for use thoroughly.
- Antibiotic therapy may be prescribed at the physician's discretion.
- The Covera™ Vascular Covered Stent should be used only by physicians who are familiar with the complications, side effects, and hazards commonly associated with dialysis access shunt revisions and endovascular procedures.

MATERIALS REQUIRED FOR A PROCEDURE USING THE COVERA™ VASCULAR COVERED STENT
- Heparinized saline
- Sterile Luer lock syringes
- Contrast medium
- 0.035 inch guidewire of appropriate length to allow safe delivery of the covered stent and removal of the delivery system
- Introducer sheath with appropriate inner diameter
- Diagnostic catheters and accessories
- Balloon angioplasty catheter for pre and/or post dilation
- Inflation device

INSTRUCTIONS FOR USE

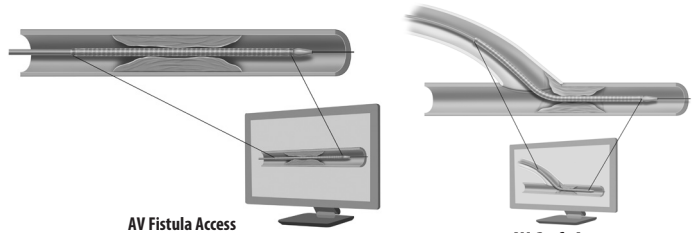
Preparation
1. After removal from the packaging, verify that the safety lock is in the locked position.
2. Using standard endovascular access techniques and fluoroscopy, access the target vessel from a site that permits the straightest possible path to the target lesion and advance an 0.035 inch guidewire across the target lesion.
3. Pre-dilate the stenosis with a PTA balloon catheter of appropriate length and diameter for the lesion to be treated.
4. Select the appropriate covered stent diameter based on the sizing table (Table 1).
5. Examine the packaging and delivery system to determine whether there is any damage or whether the sterile barrier has been compromised. Do not use the device if any of these conditions are observed.
6. Flush the delivery system through the Luer port at the proximal end of the handle with sterile saline until the saline exits the tip of the system (Figure 5).

Figure 5

Note: Do not retract the red safety lock until the covered stent is positioned across the lesion and ready to be deployed.

Delivery System Introduction
7. Under radiographic guidance, advance the delivery system over the guidewire past the target lesion and then pull back slightly on the entire system to attain correct positioning of the radiopaque markers. Use the radiopaque covered stent ends to center the covered stent across the lesion (Figure 6).

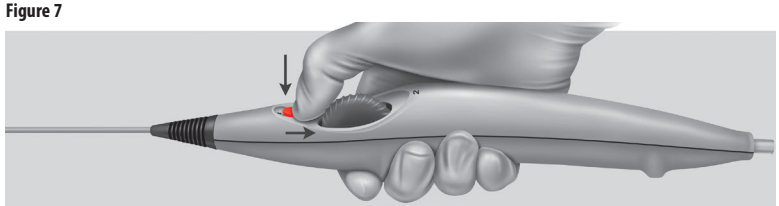
Figure 6



Note: Ensure the selected covered stent length covers the entire lesion and both ends of the implant extend at least 5 mm into the non-diseased segment of the vessel. For covered stent placements in the proximal cephalic arch select the length such that the ostial lesion is fully covered and that the proximal covered stent end does not compromise the flow in the axillary / subclavian vein. Ensure that the covered stent end extends at least 10 mm beyond the arch curvature into the straight distal cephalic vein segment. For covered stent placement in the juxta-anastomotic location of an AV fistula, careful device selection is needed to ensure that the device does not extend into the inflow artery.

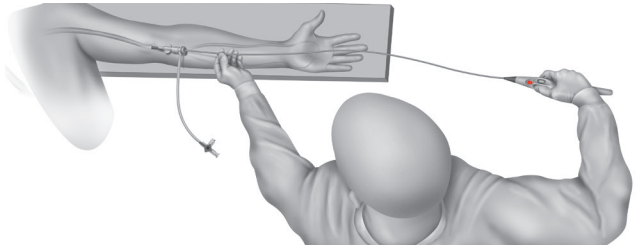
Covered Stent Deployment
8. Prior to covered stent deployment, unlock the red safety lock (Figure 7) by pressing down and pulling it back towards the end of the grip from the locked position into the unlocked position. Ensure that the red safety lock is completely retracted and that the symbol for the unlocked position is fully visible.

Figure 7



9. With your free hand, maintain a stationary hold on the white stability sheath during covered stent deployment and adjust for placement accuracy if necessary (Figure 8). Hold the white stability sheath as close as possible to the introducer without touching the dark brown moving catheter of the distal catheter assembly. Maintain the remainder of the white stability sheath (segment between left and right hand on illustration) relaxed and avoid tension.

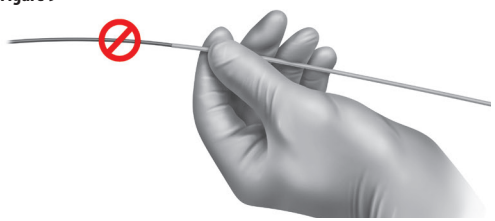
Figure 8



IMPORTANT:

Do not touch the distal catheter assembly (i.e. the dark brown catheter segment) during covered stent deployment since this may interfere with covered stent deployment and may lead to misplacement (Figure 9).

Figure 9



10. Slowly and carefully activate the covered stent release mechanism by rotating the large wheel on the top of the handle backwards.

Note: For accurate placement, subtle repositioning may be performed during initial wheel activation while the covered stent is still compressed in the catheter.
After deployment of approximately 15 mm, wait several seconds to allow the distal end of the covered stent to fully expand. Ensure the covered stent has wall apposition before completing deployment (Figure 10).

Figure 10

AV Fistula Access **AV Graft Access**

11. Complete the covered stent deployment with either the large wheel (slow release) or switch to the small wheel for faster release.

Note: Higher friction forces may occur with longer length covered stents.

12. Carefully remove the delivery system under fluoroscopy while maintaining guidewire access.
13. Post dilate the covered stent with an angioplasty balloon sized appropriately as to ensure complete wall apposition to the reference vessel. Avoid balloon dilation in the healthy, non-stenosed segment of the vein.

Note: It is recommended to advance the PTA balloon catheter through the deployed covered stent under fluoroscopy to ensure that the covered stent remains well positioned.

14. Using standard procedures, verify location and patency of the covered stent.

PATIENT IMPLANT INFORMATION CARD

A Patient Implant Information Card is provided within the product packaging.
The patient, implant and hospital information should be recorded on the card. Ensure a peel-away sticker from the product label is placed on the card before it is given to the patient. The sticker contains important information about the implant.

The patient should carry the implant information card with them and present it to any medical personnel involved in their care.

SUMMARY OF CLINICAL STUDY, AVeVA

The Covera™ Vascular Covered Stent was evaluated in the prospective, multi-center, non-randomized, single-arm, AVeVA study for the treatment of stenotic lesions at the graft-vein anastomosis of hemodialysis patients dialyzing with an AV graft. Safety and effectiveness measures of subjects receiving the Covera™ Vascular Covered Stent are presented with information derived from clinical literature as well as other prospective pivotal and post-market studies to provide clinical context for the results. A total of 181 patients were screened for eligibility of which 110 were treated with the Covera™ Vascular Covered Stent at 14 U.S. investigational sites. The primary reason for exclusion from the study was failure to meet the target lesion angiographic specific criteria. The endpoint analyses were conducted on subjects who had reached pre-specified follow-up time points: 30 days for primary safety and 6 months for effectiveness. Subjects were followed through 24 months.

Study Endpoints

The primary safety endpoint was a measure based on safety through 30 days post index procedure. Safety is defined as freedom from any adverse events (AEs) (Clinical Events Committee (CEC) adjudicated), localized or systemic, that reasonably suggests the involvement of the AV access circuit (not including stenosis or thrombosis) that require or result in any of the following alone or in combination: Additional interventions (including surgery); in-patient hospitalization or prolongation of an existing hospitalization; or death. The primary safety endpoint was evaluated against a PG of 88%.
The effectiveness endpoints of the study included measures based on Target Lesion Primary Patency (TLPP), Access Circuit Primary Patency (ACPP) and Post-intervention Secondary Patency (Secondary Patency) through 6 months post index procedure. These endpoints are presented with data from previous studies of the same indication to provide clinical context. TLPP was defined as the interval following the index intervention until the next clinically driven reintervention at or adjacent to (approximately 5 mm proximal or distal to, by visual estimation) the original treatment site or until the extremity was abandoned for permanent access. Primary patency ended when any of the following occurred: a) clinically driven reintervention in the treatment area; b) thrombotic occlusion within the treatment area; c) surgical intervention that excludes the original treatment area from the AV access circuit; and/or d) abandonment of the AV access graft due to inability to treat the original treatment area. ACPP was defined as the interval following the index intervention until the next access thrombosis or clinically driven repeated intervention. ACPP ended with a clinically driven reintervention anywhere within the access circuit; from the arterial inflow to the SVC-right atrial junction. Vessel rupture caused by PTA was not a TLPP or ACPP failure unless achieving hemostasis also caused thrombosis or required any treatment other than the study device. Secondary Patency was defined as the interval after the index intervention until the access is abandoned. Multiple repetitive treatments could be included in secondary patency.
Additional endpoints include: (1) TLPP through 30 days, 90 days, 12 months, 18 months and 24 months; (2) ACPP through 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (3) Rate of device and procedure related AEs involving the AV access circuit through 90 days, 6 months, 12 months, 18 months and 24 months; (4) Total Number of AV Access Circuit Reinterventions through 30 days, 90 days, 6 months , 12 months, 18 months and 24 months; (5) Total Number of Target Lesion Reinterventions through 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (6) Index of Patency Function (IPF) evaluated at 30 days, 90 days, 6 months , 12 months, 18 months and 24 months; (7) Index of Patency Function – Target Lesion (IPF-T) evaluated at 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (8) Secondary Patency evaluated through 30 days, 90 days, 12 months, 18 months and 24 months; (9) Acute Technical Success; and (10) Acute Procedure Success (Anatomic and Clinical Success). Information presented below includes data through 24-month follow-up.
Information was also collected regarding vessel injury, deaths, and device malfunctions.
For sample size determinations, safety at 30 days assumed a rate of 98% for subjects treated with the study device and the PG was set at 88% with attrition rate assumptions of 5%. A sample size of 109 subjects provided 104 evaluable subjects. The sample size was adequate to provide descriptive statistics related to the effectiveness and secondary endpoints as well.

Patients Studied

Eligible patients presented with a hemodynamically significant stenosis (≥ 50% by visual estimate) accompanied by a hemodynamic functional or clinical abnormality at the AV-access, graft-vein anastomosis. To be included in the study, the target lesion was required to be ≤ 9 cm in length and have a reference vessel diameter (of the adjacent, non-stenotic vessel) between 5.0 and 9.0 mm. The AV access graft had to be located in an arm, must have been implanted for ≥ 30 days, and must have undergone at least one successful dialysis session prior to the index procedure. Thrombosed and non-thrombosed grafts were included in the study.

Patients were excluded from the study if they had additional stenotic lesions (≥ 50%) in the venous outflow (> 3 cm from the edge of the target lesion) that were not successfully treated (defined as < 30% residual stenosis) prior to treating the target lesion, if they had an aneurysm or pseudoaneurysm present within the target lesion, or if they had a target lesion located such that treatment would require the Covera™ Vascular Covered Stent be deployed across the elbow joint or within a stent or stent graft.

Methods

All patients underwent a clinical evaluation at screening (prior to index procedure); treated subjects underwent a clinical evaluation prior to hospital discharge. A telephone screen to the subject and the dialysis center was performed at 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months to collect data on the AV access circuit status, AEs, reinterventions performed, and changes in applicable medications. Site investigators and dialysis centers followed their institutional procedures for hemodialysis access surveillance. Investigational sites were responsible for collecting follow-up information from subjects, dialysis centers, and any outside institutions that conducted secondary interventions on study subjects. Additionally, the majority of secondary interventions were conducted at the investigational sites. An independent CEC reviewed all AEs and performed adjudications of these events in accordance with their charter.

Results

SUBJECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Subject demographics and baseline characteristics are consistent with those in the pivotal and post market (RENOVA) studies of the Flair™ Endovascular Stent Graft. When comparing to the previous studies, specific areas of similarity include: age, sex, graft location in the left, upper arm, as well as comparable mean target lesion length and target lesion percent stenosis. The most common stent graft diameter across all studies was an 8 mm, and the most common stent graft length utilized was in the range of 40 - 60 mm. A notable difference between the studies is that only the AVeVA study included thrombosed patients. Specific demographics and baseline characteristics for the subjects enrolled in the AVeVA study are provided in Table 2 through Table 7.

Table 2: Subject Demographics, AVeVA

Age Categories	**n (%)**
< 65 years	52 (47.3)
≥ 65 and < 75 years	31 (28.2)
≥ 75 years	27 (24.5)
Sex	**n (%)**
Male	50 (45.5)
Female	60 (54.5)
Ethnicity	**n (%)**
Hispanic or Latino	24 (21.8)
Not Hispanic or Latino	86 (78.2)
Race	**n (%)**
American Indians/Alaska Native	1 (0.9)
Asian	4 (3.6)
Black or African American	44 (40.0)
White	60 (54.5)
Other	1 (0.9)
BMI Categories	**n (%)**
< 30	68 (61.8)
≥ 30	42 (38.2)

Note that n=110 subjects.

Table 3: Medical History, AVeVA

Risk Factors	**n (%)**
Subjects With at Least One Risk Factor	110 (100.0)
Diabetes - Total	72 (65.5)
Diabetes (Type 1)	4 (3.6)
Diabetes (Type 2)	68 (61.8)
Dyslipidemia	62 (56.4)
Hypertension	108 (98.2)
Cigarette Smoking - Total	43 (39.1)
Cigarette Smoking - Current	9 (8.2)
Cigarette Smoking - Former	34 (30.9)
Cardiovascular Disease	**n (%)**
Subjects With at Least One Type of Cardiovascular Disease	80 (72.7)
Congestive Heart Failure	32 (29.1)
Stroke	21 (19.1)
Coronary Artery Disease (CAD)	40 (36.4)
Myocardial Infarction (MI)	9 (8.2)
Transient Ischemic Attack (TIA)	11 (10.0)
Valvular Heart Disease	5 (4.5)
Aortic Disease	1 (0.9)
Deep Vein Thrombosis (DVT)	7 (6.4)
Peripheral Arterial/Vascular Disease (PAD) (PVD)	14 (12.7)
Atrial Fibrillation (A-Fib)	14 (12.7)
Other	33 (30.0)
Other Disease	**n (%)**
Subjects With at Least One Other Disease	105 (95.5)
Bleeding Disorder	4 (3.6)
Cancer	20 (18.2)
Steal Syndrome	1 (0.9)
Other	103 (93.6)

Note that n=110 subjects.

Table 4: Description of Access Circuit, AVeVA

Target Limb	**n (%)**
Left Arm	88 (80.0)
Right Arm	22 (20.0)
Graft Location	**n (%)**
Forearm	2 (1.8)
Upper Arm	108 (98.2)
Arterial Anastomosis	**n (%)**
Axillary	14 (12.7)
Brachial	94 (85.5)
Radial	1 (0.9)
Ulnar	1 (0.9)
Venous Anastomosis	**n (%)**
Axillary	54 (49.1)
Basilic	44 (40.0)
Brachial	9 (8.2)
Cephalic	2 (1.8)
Median Cubital	1 (0.9)

Graft Configuration	n (%)
Loop	33 (30.0)
Straight	77 (70.0)
Graft Material	**n (%)**
Bovine	10 (9.1)
ePTFE	85 (77.3)
Other	4 (3.6)
Unknown [1]	11 (10.0)
Graft Tapered?	**n (%)**
Yes	32 (29.1)
No	78 (70.9)
Graft Diameter (mm)	**N=107 [2]**
Mean (SD)	6.6 (0.77)
Min - Max	4.0 - 9.0
Thrombus Present at Index Procedure?	**n (%)**
Yes	28 (25.5)
No	82 (74.5)
Non-Target Lesions Present at Index Procedure?	**n (%)**
Yes	44 (40.0)
No	66 (60.0)

Note that N=110 subjects unless otherwise noted.

[1] For subjects whose graft material was indicated to be unknown it was verified to be nonautologous.

[2] For three (3) subjects the diameter of the graft at the time of implantation was unknown.

Table 5: Previous Index AV Access Circuit Interventions, AVeVA

	n/N (%)
Number of subjects who underwent any interventions of the index AV Access Circuit within 30 days	16/110 (14.5)
Number of Previous Interventions within 30 days prior	**n**
Total Number of Previous Interventions	22
Number of Subjects with Previous Interventions	16
Intervention	**n/n (%)**
Standard PTA	10/22 (45.5)
Thrombolysis/Thrombectomy	12/22 (54.5)
Involved Target Lesion	**n/n (%)**
Yes	16/22 (72.7)
No	6/22 (27.3)
Location	**n/n (%)**
Anastomotic	11/22 (50.0)
Basilic Vein Outflow	3/22 (13.6)
Intra-Graft	4/22 (18.2)
Subclavian Vein	1/22 (4.5)
Other	3/22 (13.6)

Note that some subjects had multiple interventions.

Table 6: Target Lesion Characteristics, AVeVA

Lesion Characteristics	n (%)
de Novo	31 (28.2)
Re-stenotic	79 (71.8)

Note that N=110 target lesions.

	N	Mean (SD)	Min-Max
Number of Lesions within Target Lesion Area	110	1.0 (0.16)	1 - 2
Target Lesion Length (mm)	110	24.1 (15.27)	2 - 70
Target Lesion Stenosis (%)	110	71.5 (14.82)	50 - 100

Table 7: Summary of Study Device* Details, AVeVA

Stent Graft Configuration	n (%)
Flared	92 (83.6)
Straight	18 (16.4)
Stent Graft Diameter	**n (%)**
7 mm	10 (9.1)
8 mm	62 (56.4)
9 mm	33 (30.0)
10 mm	5 (4.5)
Stent Graft Length	**n (%)**
40 mm	54 (49.1)
60 mm	47 (42.7)
80 mm	9 (8.2)

* Only one Covera™ Vascular Covered Stent could be implanted in each patient per the study protocol.

Subject Accountability

Investigators treated 110 subjects at 14 sites. One-hundred and eight (108) of the 110 treated subjects completed their 30-day follow-up contact. Of the two (2) subjects that did not complete their 30-day follow-up contact, one (1) subject was withdrawn due to the investigator's decision and one (1) subject died.

One-hundred and two (102) of the 110 treated subjects completed their 6-month follow-up contact. Of the six (6) additional subjects that did not complete their 6-month follow-up contact, one (1) subject was lost to follow-up and five (5) additional subjects died. Seventy-five (75) of the 110 treated subjects completed their 24-month follow-up contact. Of the thirty-five (35) subjects that did not complete their 24-month follow-up contact, one (1) subject withdrew consent; four (4) subjects were lost to follow-up; three (3) subjects were withdrawn due to the investigator's decision and twenty-seven (27) subjects died. Deaths were not considered to be related to the study device or the index procedure. The denominators used in safety and effectiveness analyses are different, and are described in respective sections.

Summary of Safety

The performance goal for the composite primary safety endpoint was met. The proportion of subjects free from primary safety events was 96.4% which met the PG of 88% (p-value=0.0021).

Table 8: Freedom from any Safety Event through 30 days (All Treated Subjects), AVeVA

Primary Safety Endpoint	Proportion n/N (%) [3]	90% CI (%) [2]	P-value [1]
Proportion Free from Primary Safety Events	106/110 (96.4)	(91.9, 98.7)	0.0021
Had Failure:			
Death	0		
Required Additional Intervention	4/110 (3.6)		
In-Patient Hospitalization or Prolongation	1/110 (0.9)		

[1] The p-value is compared to the PG (88%) and computed using the exact binomial test.

[2] 90% confidence interval is calculated using the exact binomial method.

[3] Two subjects missed the 30-day follow-up but were included in the denominator because they were followed for at least 23 days.

Note: The safety events are based on CEC adjudicated outcomes.

Four (4) subjects experienced safety events which counted as failures of the primary safety endpoint. One (1) subject experienced two (2) vessel ruptures in their AV access circuit during two (2) separate reinterventions performed after the index procedure. Another subject was reported to have an open wound infection proximal to the AV graft and as a precautionary measure their graft (and as such the previously implanted study device at the anastomosis) was explanted and discarded. A venous spasm in the axillary vein was noted in another subject, which ultimately resulted in the placement of a bare metal stent for adequate resolution. The remaining subject reported pain in their access arm during the index procedure and the subject preferred that the arm not be used for cannulation, which led to the placement of an alternate access.
A list of Safety Events observed in the Clinical Study through 24 months can be found in Table 9, and a list of CEC adjudicated device and/or procedure related AEs can be found in Table 10. AEs are defined as those that reasonably suggest the involvement of the AV access circuit (not including stenosis or thrombosis).

Table 9: Safety Events through 24 months Follow-Up (All Treated Subjects), AVeVA

AEs by Type	24 Months n (%)
Subjects With At Least One AE	**53 (48.2)**
Infusion Site Extravasation	4 (3.6)
Local Swelling	1 (0.9)
Stent Malfunction	1 (0.9)
Arteriovenous Graft Site Infection	7 (6.4)
Infected Skin Ulcer	1 (0.9)
Wound Infection	1 (0.9)
Arteriovenous Graft Aneurysm	4 (3.6)
Arteriovenous Graft Site Haematoma	1 (0.9)
Arteriovenous Graft Site Haemorrhage	3 (2.7)
Excoriation	1 (0.9)
Seroma	1 (0.9)
Skin Wound	1 (0.9)
*Vascular Graft Complication	30 (27.3)
Vascular Pseudoaneurysm	6 (5.5)
Paraesthesia	1 (0.9)
**Arteriovenous Fistula	1 (0.9)
Steal Syndrome	5 (4.5)
Vascular Dissection	2 (1.8)
Vascular Rupture	1 (0.9)
Vasospasm	1 (0.9)

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.
Note that N=110 subjects.

* Vascular Graft Complication includes events such as: access pain, AV access dysfunction, AVG dysfunction, AVG circuit issues, decreased blood flow, decreased access flow rate in AVG circuit, difficult puncture of AVG circuit, high venous pressures, increased pulsatility, infiltration of vascular access, intra-graft dissection and vessel dissection of synthetic graft, poor thrill progression and wound over upper cannulation site.

** Arteriovenous Fistula refers to a site reported event of an abnormal connection from the arteriovenous graft near the arterial anastomosis to the brachial vein.

Table 10: CEC Adjudicated Device and/or Procedure Related Adverse Events through 24 months (inclusive of reported Safety Events in Table 9) (All Treated Subjects), AVeVA

AEs by Type	Device Related			Procedure Related		
	Definitely n (%)	Possibly n (%)	Not Related n (%)	Definitely n (%)	Possibly n (%)	Not Related n (%)
Subject with at Least One AE	**1 (0.9)**	**9 (8.2)**	**43 (39.1)**	**3 (2.7)**	**5 (4.5)**	**45 (40.9)**
Infusion Site Extravasation	1 (0.9)	0	3 (2.7)	0	0	4 (3.6)
Local Swelling	0	0	1 (0.9)	0	0	1 (0.9)
Stent Malfunction	0	0	1 (0.9)	0	0	1 (0.9)
Arteriovenous Graft Site Infection	0	2 (1.8)	5 (4.5)	0	1 (0.9)	6 (5.5)
Infected Skin Ulcer	0	0	1 (0.9)	0	0	1 (0.9)
Wound Infection	0	0	1 (0.9)	0	0	1 (0.9)
Arteriovenous Graft Aneurysm	0	0	4 (3.6)	0	0	4 (3.6)
Arteriovenous Graft Site Haematoma	0	0	1 (0.9)	0	0	1 (0.9)
Arteriovenous Graft Site Haemorrhage	0	0	3 (2.7)	0	0	3 (2.7)
Excoriation	0	0	1 (0.9)	0	0	1 (0.9)
Seroma	0	0	1 (0.9)	0	0	1 (0.9)
Skin Wound	0	0	1 (0.9)	0	0	1 (0.9)
*Vascular Graft Complication	0	3 (2.7)	27 (4.5)	2 (1.8)	1 (0.9)	27 (24.5)
Vascular Pseudoaneurysm	0	1 (0.9)	5 (4.5)	0	0	6 (5.5)
Paraesthesia	0	1 (0.9)	0	0	1 (0.9)	0
Arteriovenous Fistula	0	0	1 (0.9)	0	0	1 (0.9)
Steal Syndrome	0	2 (1.8)	3 (2.7)	0	3 (2.7)	2 (1.8)
Vascular Dissection	0	0	2 (1.8)	0	0	2 (1.8)
Vascular Rupture	0	0	1 (0.9)	0	0	1 (0.9)
Vasospasm	0	1 (0.9)	0	1 (0.9)	0	0

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.
Note that N=110 Subjects.

* The three events associated with Vascular Graft Complication were reported as access pain. One of the events was adjudicated as possibly related to device and procedure, and the other two were adjudicated as possibly related to device and definitely related to procedure.

Summary of Effectiveness

Effectiveness was evaluated using multiple endpoints, with TLPP being an important endpoint as it was used as the primary endpoint for previous studies of the same indication. To provide clinical context, the 6-month TLPP rates from the pivotal and post market (RENOVA) studies of the Flair™ Endovascular Stent Graft, are provided in Table 11 below. The results of the AVeVA study demonstrate that the TLPP rates for the Covera™ Vascular Covered Stent are similar to results from the study device arm of the previous studies and greater than the patency rates for PTA from these studies.

Table 11: TLPP Rates in AV Grafts at 6 Months, AVeVA

Study	N	Study Device	90% Confidence Intervals	Randomized PTA	90% Confidence Intervals
Flair™ Pivotal Study	91	51%*	(42%, 60%)	23% (N=86)	(16%, 32%)
RENOVA Study (Flair™)	138	66%	(59%, 73%)	40% (N=132)	(33%, 48%)
AVeVA Study (Covera™ Vascular Covered Stent)	**100****	**71%**	**(61%, 80%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" patients using the Flair™ Endovascular Stent Graft, resulting in a 60% TLPP rate for those patients at 6 months.

** Nine subjects were excluded from the denominator due to discontinuation or abandonment of the index AV access circuit prior to day 150 of their follow-up. One additional subject was excluded due to a major protocol deviation; refer to Table 17, Footnote [1] for additional detail.

Figure 11 presents the Kaplan-Meier curve for TLPP through 6 months for all treated subjects.

Figure 11: Kaplan-Meier Analysis of TLPP (All Treated Subjects), AVeVA

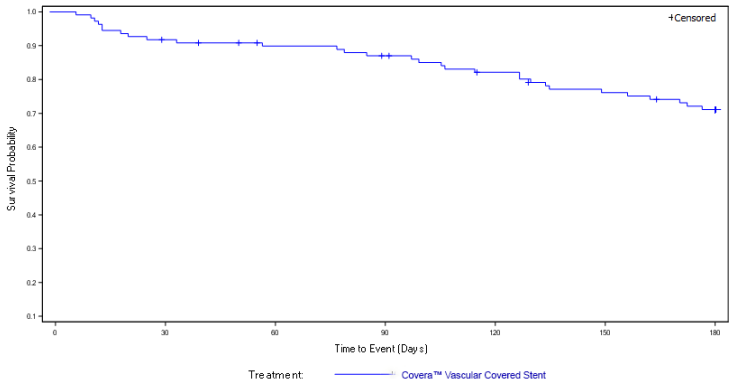


Table 12: Kaplan-Meier Analysis of TLPP (All Treated Subjects), AVeVA

Time Point	# of Subjects Left	# of Subjects Censored	# of Subjects with TLPP Failure	TLPP Rate (95% CI) [1]
30 Days	99	1	9	91.7% (84.7% , 95.6%)
90 Days	90	5	14	87.0% (79.0% , 92.1%)
180 Days	70	9	30	71.1% (61.3% , 78.8%)

[1] The rates are estimated using the Kaplan-Meier method and the 95% confidence intervals are estimated using Greenwood's formula.

ACPP and secondary patency are also important effectiveness endpoints evaluated in this study. ACPP and secondary patency are inclusive of all patency events including those that occurred at the target lesion (i.e. inclusive of TLPP). The 6-month ACPP and secondary patency rates from the pivotal and post market (RENOVA) studies of the Flair™ Endovascular Stent Graft are provided in Table 13 and Table 14 below. The results of the AVeVA study demonstrate that the ACPP rates for the Covera™ Vascular Covered Stent are similar to results from the study device arm of the previous studies and greater than the ACPP rates for PTA from these studies. Furthermore, the secondary patency rates are proportionate for the study devices across these studies.

Table 13: ACPP Rates in AV Grafts at 6 Months, AVeVA

Study	N	Study Device	95% Confidence Intervals	Randomized PTA	95% Confidence Intervals
Flair™ Pivotal Study	91	38%*	(28%, 49%)	20% (N=86)	(12%, 30%)
RENOVA Study (Flair™)	138	41%	(33%, 50%)	25% (N=132)	(18%, 33%)
AVeVA Study (Covera™ Vascular Covered Stent)	**101****	**40%**	**(30%, 50%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" patients using Flair™ Endovascular Stent Graft, resulting in a 43% ACPP rate for those patients at 6 months

** One subject from the ten excluded from TLPP Was included in the ACPP analysis because the subject was a failure for ACPP only.

Table 14: Secondary Patency Rates in AV Grafts at 6 Months, AVeVA

Study	N	Study Device	95% Confidence Intervals	Randomized PTA	95% Confidence Intervals
Flair™ Pivotal Study	91	81%*	(72%, 89%)	86% (N=85)	(77%, 92%)
RENOVA Study (Flair™)	138	75%	(67%, 82%)	79% (N=132)	(71%, 85%)
AVeVA Study (Covera™ Vascular Covered Stent)	**100****	**92%**	**(85%, 97%)**	-	-

* Physicians unfamiliar with the study device enrolled "roll-in" patients before starting the randomized phase of the trial. This resulted in 37 "roll-in" patients using the Flair™ Endovascular Stent Graft patients, resulting in a 91% secondary patency rate for those patients at 6 months

** Nine subjects were excluded from the denominator due to discontinuation or abandonment. One additional subject was excluded due to a major protocol deviation; refer to Table 17, Footnote [1] for additional detail.

Subgroup analyses were performed on evaluable subjects (Table 15). Per these analyses it is likely that there are no differences in effectiveness outcomes for sex, race, age, target lesion characteristics, outflow vessel, and presence of secondary lesion(s). A difference that is likely significant was observed between subjects that presented with thrombosis at the time of the index procedure comparing to subjects without thrombosis (p-value 0.0169, note this is not adjusted for multiplicity) where subjects presenting with thrombosis were observed to have 50.0% TLPP versus 76.9% TLPP for the non-thrombotic group. A similar trend between the two subgroups of subjects was also observed when subjects that had been treated for thrombosis within 30 days of the index procedure were included (multiplicity unadjusted p-value 0.0418).

Table 15: Analysis of TLPP at 6 Months by Subgroup (All Treated Subjects), AVeVA

Subgroup	Proportion n/N (%)	95% CI (%) [2]	P-Value [1]
Target Lesion Characteristics			
de novo	17/26 (65.4)	(44.3, 82.8)	0.4644
Re-stenotic	54/74 (73.0)	(61.4, 82.6)	
Outflow Vessel			
Axillary Vein	33/49 (67.3)	(52.5, 80.1)	0.2914
Basilic Vein	31/40 (77.5)	(61.5, 89.2)	
Presence of Secondary Lesion(s)			
Yes	26/40 (65.0)	(48.3, 79.4)	0.2821
No	45/60 (75.0)	(62.1, 85.3)	
Presence of Thrombus Prior to Treatment at Index Procedure			
Yes	11/22 (50.0)	(28.2, 71.8)	0.0169
No	60/78 (76.9)	(66.0, 85.7)	
Presence of Thrombus at and /or within 30 days of Index Procedure			
Yes	15/27 (55.6)	(35.3, 74.5)	0.0418
No	56/73 (76.7)	(65.4, 85.8)	

[1] P-values are calculated using the chi-squared test and are not adjusted for multiplicity.
[2] The 95% confidence interval is calculated using the exact binomial method. Confidence intervals are unadjusted for multiple comparisons.

The subgroup analysis for ACPP for subjects that presented with thrombosis at the time of the index procedure and within 30 days prior to the index procedure is shown in Table 16.

Table 16: ACPP by Subgroup at 6 months of Follow-Up (All Treated Subjects), AVeVA

Subgroup	Proportion n/N (%)	95% CI (%) [2]	P-Value [1]
Presence of Thrombus Prior to Treatment at Index Procedure			
Yes	7/23 (30.4)	(13.2, 52.9)	0.3092
No	33/78 (42.3)	(31.2, 54.0)	
Presence of Thrombus at and /or within 30 days of Index Procedure			
Yes	9/28 (32.1)	(15.9, 52.4)	0.3442
No	31/73 (42.5)	(31.0, 54.6)	

[1] P-values are calculated using the chi-squared test and are not adjusted for multiplicity.
[2] The 95% confidence interval is calculated using the exact binomial method. Confidence intervals are unadjusted for multiple comparisons.

ADDITIONAL ENDPOINTS

Table 17 presents information on additional endpoints with proportional values for all follow-up time points at 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months. Acute Technical Success was defined as successful deployment, based on the operator's opinion, of the implant to the intended location assessed at the time of the index procedure. Procedure Success was defined as anatomic success and resolution of the pre-procedural clinical indicator(s) (clinical success) of a hemodynamically significant stenosis as further defined by Anatomic and Clinical Success. Anatomic Success was determined during the primary procedure and was defined as the achievement of a post-procedure residual stenosis of less than or equal to 30%, measured at the narrowest point of the lumen when compared to the adjacent non-stenosed venous segment. Whereas Clinical Success was defined as resolution of pre-procedural clinical indicators of access malfunction in the opinion of the investigator prior to hospital discharge which could include an abnormal physical exam, abnormal pressure monitoring parameters, decreased access flow, difficulty with dialysis needle puncture, pulling thrombus, prolonged bleeding, increased recirculation, and/or inadequate dialysis clearance.

Table 17: Additional Endpoints, Proportional Values (All Treated Subjects), AVeVA

	Procedure n/N (%)	30 days n/N (%)	90 days n/N (%)	6 months n/N (%)	12 months n/N (%)	18 months n/N (%)	24 months n/N (%)
Acute Technical Success [1]	110/110 (100)	N/A	N/A	N/A	N/A	N/A	N/A
Acute Procedure Success [1]	110/110 (100)	N/A	N/A	N/A	N/A	N/A	N/A
TLPP	N/A	100/109 (91.7%)	91/105 (86.7%)	71/101 (70.3%)	46/91 (50.5%)	33/86 (38.4%)	25/83 (30.1%)
ACPP	N/A	96/109 (88.1%)	72/106 (67.9%)	40/102 (39.2%)	14/97 (14.4%)	7/94 (7.4%)	4/94 (4.3%)
Secondary Patency	N/A	107/109 (98.2%)	101/105 (96.2%)	93/101 (92.1%)	76/89 (85.4%)	64/80 (80.0%)	53/72 (73.6%)
Proportion Free From Device and Procedure Related AEs [2]	N/A	105/110 (95.5%)	99/108 (91.7%)	96/105 (91.4%)	85/96 (88.5%)	77/88 (87.5%)	69/80 (86.3%)

[1] One (1) subject presented with a clotted graft at the time of the index procedure and a 100% stenosis at the target lesion. During the initial inflation of the target lesion, rupture of the vessel occurred. After the urgency of resolving the rupture had passed, the investigator determined that there was an additional lesion about 1 cm peripheral to the stent graft. Because the first target lesion segment was stenosed to 100%, it is unlikely the additional lesion would have been seen until after pre-dilatation. A major protocol deviation was required as the remaining segment had to be treated with an adjunctive therapy as placement of a secondary study device in an overlapped configuration was not allowed per the protocol. This deviation does not implicate the technical and procedural success of the device as the study device was placed as initially intended as assessed by the investigator, however the subject was excluded from the follow-up patency analysis due to the major protocol deviation.

[2] Refer to Table 10 for a complete list of device and procedure related AEs at 24 months.

Table 18 presents information on additional endpoints with mean values for all follow-up time points at 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months. Total Number of AV Access Circuit Reinterventions was defined as the number of reinterventions to the AV access circuit until access abandonment or through study completion. Total Number of Target Lesion Reinterventions was defined as the number of reinterventions to maintain target lesion patency. Index of Patency Function (IPF) was defined as the time from the index study procedure to study completion or access abandonment divided by the number of visits for reinterventions performed on the AV access circuit in order to maintain vascular access for hemodialysis. A visit was defined as one (1) procedural event, regardless of the number or type of interventions performed during the visit. The index procedure was counted as the first visit to ensure all subjects have a denominator of at least one. Index of Patency Function – Target Lesion (IPF-T) was defined as the time from the index study procedure to study completion or complete access abandonment divided by the number of visits for a reintervention performed at the target lesion in order to maintain vascular access for hemodialysis.

Table 18: Additional Endpoints, Mean Values (All Treated Subjects), AVeVA

Total Number of AV Access Circuit Reinterventions	n	mean (SD)*
30 Days	16	0.15 (0.450)
90 Days	51	0.49 (0.774)
6 Months	111	1.10 (1.237)
12 Months	222	2.31 (2.221)
18 Months	284	3.05 (2.783)
24 Months	333	3.58 (3.090)
Total Number of Target Lesion Reinterventions	**n**	**mean (SD)***
30 Days	10	0.09 (0.350)
90 Days	18	0.17 (0.511)
6 Months	44	0.44 (0.783)
12 Months	81	0.91 (1.411)
18 Months	100	1.25 (1.768)
24 Months	116	1.55 (1.933)
Index of Patency Function (days)	**mean (SD)**	
30 Days	28.10 (5.446)	
90 Days	72.24 (26.01)	
6 Months	110.3 (57.71)	
12 Months	144.3 (102.6)	
18 Months	163.1 (131.6)	
24 Months	177.9 (153.2)	
Index of Patency Function – Target Lesion (days)	**mean (SD)**	
30 Days	28.75 (4.475)	
90 Days	83.27 (18.48)	
6 Months	146.3 (52.30)	
12 Months	253.2 (127.3)	
18 Months	325.7 (197.3)	
24 Months	380.3 (270.7)	

* Mean (SD) is the average number of reinterventions per subject.

Vessel Ruptures

During the index procedure, two (2) subjects experienced vessel rupture at the target lesion during pre-dilation prior to study device implantation. The protocol allowed for vessel rupture at the target lesion to be treated using the study device and as such, the ruptures were resolved after implantation of the Covera™ Vascular Covered Stent. The investigators deemed the procedures a success and no further AEs were reported for these subjects.

Summary of Deaths

There were twenty-six (26) deaths (23.6%) reported in the 24-month follow-up period. Ten (10) deaths were cardiac-related, five (5) were due to voluntary termination of dialysis, and four (4) subjects expired with primary cause reported by the site as unknown. The remaining causes of death were reported as sepsis (3), pneumonia (1), volume overload (1), multiple organ failure due to calciphylaxis (1), and worsening terminal cerebrovascular disease (1). Deaths were not considered to be related to the study device or index procedure.

Observed Device Malfunctions

There were zero (0) device malfunctions reported.

Conclusions Drawn from Pre-specified Endpoints

The prospective, multi-center, non-randomized, single-arm study of the Covera™ Vascular Covered Stent in the treatment of stenotic lesions at the graft-vein anastomosis of hemodialysis patients dialyzing with an AV graft (AVeVA) evaluated safety and effectiveness measures.

The proportion of subjects free from primary safety events at 30-days was 96.4%, meeting the performance goal of 88% (p-value=0.0021). Additionally, results from the study demonstrate a TLPP rate of 71.0% at 6-months.

Data from the clinical trial provide a reasonable assurance that the Covera™ Vascular Covered Stent is safe and effective for the treatment of stenoses at the venous anastomosis of ePTFE or other synthetic arterio-venous (AV) access grafts when used in accordance with its labeling.

SUMMARY OF CLINICAL STUDY, AVeNEW IDE

The Covera™ Vascular Covered Stent was evaluated in the prospective, multi-center, randomized, concurrently-controlled AVeNEW clinical study designed to assess the safety and effectiveness of the Covera™ Vascular Covered Stent for the treatment of stenotic lesions in the upper extremity venous outflow of the AV access circuit of hemodialysis subjects dialyzing with an AV fistula. The study compares the use of Covera™ Vascular Covered Stent (following PTA) to PTA alone.

A total of 280 subjects were randomized into the AVeNEW study at 24 global sites with one hundred forty two (142) randomized to Covera™ Vascular Covered Stent (following standard PTA) and one hundred thirty eight (138) randomized to standard PTA. The endpoint analyses were conducted on subjects who had reached pre-specified follow-up time points: 30 days for primary safety and 6 months for primary effectiveness. Subjects were followed through 24 months.

Study Endpoints

The primary safety endpoint is a measure based on safety through 30 days post-index procedure. Safety is defined as freedom from any adverse event(s) (AEs), localized or systemic, that reasonably suggest(s) the involvement of the AV access circuit (not including stenosis or thrombosis) and that require(s) or result(s) in any of the following alone or in combination: additional interventions (including surgery); in-patient hospitalization or prolongation of an existing hospitalization; or death. The primary safety endpoint in the Covera™ Vascular Covered Stent group is evaluated against that observed in the PTA group.

The primary effectiveness endpoint of the study is based on Target Lesion Primary Patency (TLPP) at 6 months post-index procedure. TLPP is defined as the interval following the index intervention until the next clinically driven reintervention at or adjacent to (approximately 5 mm proximal and distal to, by visual estimation) the original treatment site or until the extremity is abandoned for permanent access. Primary patency ends when any of the following occurs: a) clinically driven reintervention in the treatment area; b) thrombotic occlusion within the treatment area; c) surgical intervention that excludes the original treatment area from the AV access circuit, and/or d) abandonment of the AV fistula due to inability to treat the original treatment area. Vessel rupture at the target lesion caused by PTA is not a TLPP failure unless achieving hemostasis also causes thrombosis or requires any treatment other than what the patient has been randomized to receive. The primary effectiveness endpoint in the Covera™ Vascular Covered Stent group is evaluated against that observed in the PTA group.

The study included two secondary endpoints with hypothesis testing, which are TLPP through 12 months and Access Circuit Primary Patency (ACPP) through 6 months. ACPP was defined as the interval following the index intervention until the next access thrombosis or clinically driven repeated intervention. ACPP ended with a clinically driven reintervention anywhere within the access circuit; from the arterial inflow to the SVC-right atrial junction. Vessel rupture caused by PTA was not an ACPP failure unless achieving hemostasis also caused thrombosis. Evaluation of the secondary endpoints with hypothesis testing is performed in a hierarchical fashion in the order listed.

Additional endpoints include: (1) TLPP through 30 days, 90 days, 18 months, and 24 months; (2) ACPP through 30 days, 90 days, 12 months, 18 months, and 24 months; (3) Rate of device and procedure related AEs involving the AV access circuit through 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months; (4) Total Number of AV Access Circuit Reinterventions through 30 days, 90 days, 6 months , 12 months, 18 months, and 24 months; (5) Total Number of Target Lesion Reinterventions through 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months; (6) Index of Patency Function (IPF) evaluated at 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months; (7) Index of Patency Function – Target Lesion (IPF-T) evaluated at 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months; (8) Secondary Patency evaluated through 30 days, 90 days, 6 months, 12 months, 18 months, and 24 months; (9) Acute Technical Success; and (10) Acute Procedure Success (Anatomic and Clinical Success).

Patients Studied

Eligible subjects had a hemodynamically significant stenosis (≥ 50% by visual estimate) in the venous outflow of the AV access circuit and presented with clinical or hemodynamic evidence of AV fistula dysfunction. To be included in the study, the target lesion was required to be ≤ 9 cm in length and have a reference vessel diameter (of the adjacent, non-stenotic vessel) between 5.0 and 9.0 mm. The AV fistula had to be located in an upper extremity and have undergone at least one successful dialysis session prior to the index procedure.

Patients were excluded from the study if they had additional stenotic lesions (≥ 50%) in the venous outflow (> 3 cm from the edge of the target lesion) that were not successfully treated (defined as ≤ 30% residual stenosis) prior to treating the target lesion, if they had an aneurysm or pseudoaneurysm present within the target lesion, or if they had a target lesion located such that treatment would require the Covera™ Vascular Covered Stent be deployed across the elbow joint, within a stent or stent graft, in the central veins (subclavian, brachiocephalic, superior vena cava (SVC)), or across the segment of fistula utilized for dialysis needle puncture (i.e. "cannulation zone").

Methods

All subjects underwent a clinical evaluation at screening (prior to index procedure); treated subjects underwent a clinical evaluation prior to hospital discharge. A telephone contact to the subject and the dialysis center was performed at 30 days, 90 days, 6 months, and 12 months with a required office visit to the investigational site at 6 months to collect data on the AV access circuit status, overall health of the subject and access function via a clinical exam, AEs, reinterventions performed, and changes in applicable medications. Investigational sites and dialysis centers followed their institutional procedures for hemodialysis access surveillance. Investigational sites were responsible for collecting follow-up information from subjects, dialysis centers, and any outside institutions that conducted secondary interventions on study subjects. Additionally, the majority of secondary interventions were conducted at the investigational sites. An independent CEC reviewed all AEs and performed adjudications of these events in accordance with their charter.

The Intent to Treat (ITT) population consists of all enrolled subjects who have signed the informed consent form and have been randomized to receive either Covera™ Vascular Covered Stent or PTA alone. The Modified ITT (mITT) population consists of any subjects in the ITT population who are treated with the Covera™ Vascular Covered Stent (following PTA) or PTA alone. Subjects that were treated with an adjunctive treatment such as bare metal stent or stent graft (other than study device Covera™ Vascular Covered Stent) during the study index procedure are excluded from the mITT population. The Per-Protocol population consists of subjects in the mITT population who do not have any major protocol deviations. The protocol deviations that are considered to have a "major" grade were defined a priori. All efficacy analyses are primarily based on the mITT population.

Results

Subject Demographics and Baseline Characteristics

Demographic and background characteristics for the ITT population are provided in Table 19 below. The majority of subjects were white (68.6%) and male (61.8%). The mean age at the time of the index procedure was 63 ± 12.4 years and there was no difference between the two treatment arms with regards to age. A summary of relevant medical risk factors as well as selected medical history background for the ITT population is provided in Table 20. The expected co-morbidities for this population were observed, with nearly all of the subjects being hypertensive (97.1%), three quarter (75.4%) diabetic, and 67.9% having cardiovascular disease. There were no differences noted between the two treatment arms for demographics or any of the relevant medical risk factors.

Table 19: Subject Demographics (ITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280	P-value
Age Categories	**n (%)**	**n (%)**	**n (%)**	**0.1945**
< 65 years	79 (55.6)	76 (55.1)	155 (55.4)	
≥ 65 and < 75 years	36 (25.4)	45 (32.6)	81 (28.9)	
≥ 75 years	27 (19.0)	17 (12.3)	44 (15.7)	
Sex	**n (%)**	**n (%)**	**n (%)**	**0.7558**
Male	89 (62.7)	84 (60.9)	173 (61.8)	
Female	53 (37.3)	54 (39.1)	107 (38.2)	
Ethnicity	**n (%)**	**n (%)**	**n (%)**	**0.3776**
Hispanic or Latino	48 (33.8)	54 (39.1)	102 (36.4)	
Not Hispanic or Latino	93 (65.5)	84 (60.9)	177 (63.2)	
Missing	1 (0.7)	0	1 (0.4)	
Race	**n (%)**	**n (%)**	**n (%)**	**0.0819**
Asian	0	6 (4.3)	6 (2.1)	
Native Hawaiian or Other Pacific Island	2 (1.4)	0	2 (0.7)	
Black or African American	36 (25.4)	36 (26.1)	72 (25.7)	
White	100 (70.4)	92 (66.7)	192 (68.6)	
Other	4 (2.8)	4 (2.9)	8 (2.9)	
BMI Categories	**n (%)**	**n (%)**	**n (%)**	**0.0108**
< 30	68 (47.9)	87 (63.0)	155 (55.4)	
≥ 30	74 (52.1)	51 (37.0)	125 (44.6)	

Table 20: Medical History (ITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280	
Risk Factors	**n (%)**	**n (%)**	**n (%)**	**P value**
Subjects With at Least One Risk Factor	141 (99.3)	136 (98.6)	277 (98.9)	0.5449
Diabetes - Total	108 (76.1)	103 (74.6)	211 (75.4)	0.7830
Diabetes (Type 1)	7 (4.9)	9 (6.5)	16 (5.7)	
Diabetes (Type 2)	101 (71.1)	94 (68.1)	195 (69.6)	
Dyslipidemia	95 (66.9)	85 (61.6)	180 (64.3)	0.3541
Hypertension	139 (97.9)	133 (96.4)	272 (97.1)	0.4481
Cigarette Smoking - Total	62 (43.7)	62 (44.9)	124 (44.3)	0.8312
Cigarette Smoking - Current	8 (5.6)	15 (10.9)	23 (8.2)	
Cigarette Smoking - Former	54 (38.0)	47 (34.1)	101 (36.1)	
Cardiovascular Disease	**n (%)**	**n (%)**	**n (%)**	***P* value**
Subjects With at Least One Type of Cardiovascular Disease	95 (66.9)	95 (68.8)	190 (67.9)	0.7283
Congestive Heart Failure	35 (24.6)	40 (29.0)	75 (26.8)	0.4125
NYHA Class I	1 (0.7)	2 (1.4)	3 (1.1)	
NYHA Class II	2 (1.4)	1 (0.7)	3 (1.1)	
NYHA Class UNKNOWN	32 (22.5)	37 (26.8)	69 (24.6)	
Stroke	20 (14.1)	24 (17.4)	44 (15.7)	0.4472
Coronary Artery Disease (CAD)	46 (32.4)	52 (37.7)	98 (35.0)	0.3538
Myocardial Infarction (MI)	22 (15.5)	18 (13.0)	40 (14.3)	0.5581
Transient Ischemic Attack (TIA)	2 (1.4)	7 (5.1)	9 (3.2)	0.0822
Valvular Heart Disease	6 (4.2)	4 (2.9)	10 (3.6)	0.5498
Aortic Disease	2 (1.4)	4 (2.9)	6 (2.1)	0.3893
Deep Vein Thrombosis (DVT)	5 (3.5)	4 (2.9)	9 (3.2)	0.7678
Peripheral Arterial/Vascular Disease (PAD) (PVD)	24 (16.9)	29 (21.0)	53 (18.9)	0.3797
Atrial Fibrillation (A-Fib)	15 (10.6)	16 (11.6)	31 (11.1)	0.7834
Other	38 (26.8)	37 (26.8)	75 (26.8)	0.9923
Other Disease	**n (%)**	**n (%)**	**n (%)**	***P* value**
Subjects With at Least One Other Disease	129 (90.8)	129 (93.5)	258 (92.1)	0.4130
Bleeding Disorder	3 (2.1)	3 (2.2)	6 (2.1)	0.9718
Cancer	17 (12.0)	15 (10.9)	32 (11.4)	0.7719
Steal Syndrome	2 (1.4)	1 (0.7)	3 (1.1)	0.5785
Other	128 (90.1)	126 (91.3)	254 (90.7)	0.7373

A summary of characteristics of the AV access circuit as reported by sites is shown in Table 21. The majority of subjects had upper arm access in the left arm with inflow provided by the brachial artery and outflow through the cephalic vein. The type of fistula configuration was matched between the study arms with slight majority (57.9%) having brachiocephalic access, and an additional 22.9% having a transposed brachiobasilic fistula. Overall, 28.2% of the subjects had a vein transposed to facilitate the fistula configuration.

Table 21: Description of Access Circuit, AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280
	n (%)	**n (%)**	**n (%)**
Target Limb			
Left Arm	106 (74.6)	110 (79.7)	216 (77.1)
Right Arm	36 (25.4)	28 (20.3)	64 (22.9)
Access Position			
Forearm	9 (6.3)	8 (5.8)	17 (6.1)
Upper Arm	132 (93.0)	130 (94.2)	262 (93.6)
Other	1 (0.7)	0	1 (0.4)
Inflow Artery			
Axillary	2 (1.4)	2 (1.4)	4 (1.4)
Brachial	128 (90.1)	127 (92.0)	255 (91.1)
Radial	12 (8.5)	9 (6.5)	21 (7.5)
Outflow Vein			
Axillary	2 (1.4)	1 (0.7)	3 (1.1)
Basilic	35 (24.6)	42 (30.4)	77 (27.5)
Cephalic	105 (73.9)	95 (68.8)	200 (71.4)
Fistula Configuration			
Radiocephalic	12(8.5)	9(6.5)	21(7.5)
Brachiocephalic	84(59.2)	78(56.5)	162(57.9)
Transposed Brachiobasilic	27(19.0)	37(26.8)	64(22.9)
All Other	19(13.4)	14(10.1)	33(11.8)
Transposed?			
Yes	36 (25.4)	43 (31.2)	79 (28.2)
No	106 (74.6)	95 (68.8)	201 (71.8)

Interventions within 30 days prior to the index procedure on the index AV access circuit are shown in Table 22. A total of 10 interventions were performed in eight (8) subjects (2.9%) in the index AV access circuit within 30 days of being enrolled in this study. The majority of these interventions involved the target lesion (8 of 280, 2.9%) and comprised of PTA (8) and thrombolysis and/or thrombectomies (1).

Table 22: Previous Index AV Access Circuit Interventions, AVeNEW IDE

	Covera™ Vascular Covered Stent N=142	PTA Alone N=138	Total N=280
	n/N (%)	**n/N (%)**	**n/N (%)**
Number of subjects who underwent any interventions of the index AV Access Circuit within 30 days prior to the index procedure	4/142 (2.8)	4/138 (2.9)	8/280 (2.9)
Number of subjects planning to undergo any interventions of the index AV Access Circuit within 30 days	0	0	0
Number of Previous Interventions	**n**	**n**	**n**
Total Number of Previous Interventions	5	5	10
Number of Subjects with Previous Interventions	4	4	8
Mean (SD)	1.3 (0.50)	1.3 (0.50)	1.3 (0.46)

Note: Some subjects had multiple interventions.

Site-reported baseline target lesion characteristics are shown in Table 23 and Table 24. The majority of lesions (73.2%) were re-stenotic in nature and a majority of the anastomoses (72.9%) were at the cephalic vein, with the majority of stenosis located at the cephalic vein arch (52.9%).

The reference vessel diameter averaged 8.1 ± 1.14 mm, the target lesion length ranged from 2 to 80 mm, with a stenosis of 72.5 ± 12.5% on average by visual estimate.

Table 23: Target Lesion Characteristics (ITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280
De Novo Lesion?	**n (%)**	**n (%)**	**n (%)**
Yes	35 (24.6)	40 (29.0)	75 (26.8)

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280
No	107 (75.4)	98 (71.0)	205 (73.2)
Vessel	**n (%)**	**n (%)**	**n (%)**
Axillary Vein	3 (2.1)	2 (1.4)	5 (1.8)
Basilic Vein	30 (21.1)	35 (25.4)	65 (23.2)
Cephalic Vein	108 (76.1)	96 (69.6)	204 (72.9)
Other	1 (0.7)	5 (3.6)	6 (2.1)
Lesion Location	**n (%)**	**n (%)**	**n (%)**
Axillary Vein	3 (2.1)	2 (1.4)	5 (1.8)
Basilic Vein Outflow	13 (9.2)	15 (10.9)	28 (10.0)
Basilic Vein Swing Point	16 (11.3)	18 (13.0)	34 (12.1)
Cephalic Vein Arch	78 (54.9)	70 (50.7)	148 (52.9)
Cephalic Vein Outflow	25 (17.6)	24 (17.4)	49 (17.5)
Forearm Venous Outflow	3 (2.1)	2 (1.4)	5 (1.8)
Juxta-Anastomotic	2 (1.4)	0	2 (0.7)
Other	2 (1.4)	7 (5.1)	9 (3.2)

Table 24: Angiographic Target Lesion Characteristics (ITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Reference Vessel Diameter (mm)	8.1 (1.35)	8.0 (0.87)	8.1 (1.14)
Target Lesion Length (mm)	28.8 (17.40)	29.7 (16.98)	29.3 (17.17)
Target Lesions Stenosis (%)	72.5 (12.40)	72.5 (12.65)	72.5 (12.50)

Table 25: Summary of Study Device* Details (As Treated Population), AVeNEW IDE

	Covera™ Vascular Covered Stent N = 141
Stent Graft Configuration	**n (%)**
Flared	65 (46.1)
Straight	76 (53.9)
Stent Graft Diameter	**n (%)**
6 mm	1 (0.7)
7 mm	4 (2.8)
8 mm	26 (18.4)
9 mm	42 (29.8)
10 mm	68 (48.2)
Stent Graft Length	**n (%)**
30 mm	3 (2.1)
40 mm	59 (41.8)
60 mm	52 (36.9)
80 mm	23 (16.3)
100 mm	4 (2.8)
Placement Configuration	**n (%)**
Single Stent Graft Only	140 (99.3)
Other	1 (0.7)
Was Placement Successful at intended site?	
Yes	141 (100)

* Although only one Covera™ Vascular Covered Stent could be implanted per the study protocol, in one subject, a second Covera™ Vascular Covered Stent was placed in an overlap configuration during the index procedure.

The protocol and IFU required pre-dilation of the target lesion and successful effacement of the angioplasty balloon to meet the final eligibility criterion. Residual stenosis ranged from 0.0 to 90% where 54 subjects (19.3%) were reported to have an unsuccessful pre-dilation (defined as a residual stenosis of >30%). Of which, 33 subjects (23.2%) were randomized to Covera™ Vascular Covered Stent post PTA and 21 subjects (15.2%) were randomized to PTA. A summary of the pre-dilation details is provided in Table 26.

Table 26: Target Lesion Pre-Dilatation, AVeNEW IDE

	Covera™ Vascular Covered Stent N = 142	PTA Alone N = 138	Total N = 280
	Mean (SD)	**Mean (SD)**	**Mean (SD)**
Balloon Diameter (mm)	8.5 (1.03)	8.4 (1.11)	8.5 (1.07)
Balloon Length (mm)	46.8 (14.85)	49.0 (16.75)	47.9 (15.83)
Number of Balloon Inflations	1.3 (0.56)	1.3 (0.59)	1.3 (0.58)
Maximum Pressure of Balloon Inflation (atm)	20.6 (5.38)	21.2 (5.78)	20.9 (5.58)
Total Duration of Inflation (sec)	43.4 (52.83)	41.2 (40.96)	42.3 (47.28)
Residual Stenosis (%)	21.7 (20.52)	15.4 (16.58)	18.6 (18.91)

Subject Accountability

A total of 280 subjects were randomized into the AVeNEW study at 24 global sites with one hundred forty-two (142) randomized to Covera™ Vascular Covered Stent (following standard PTA) and one hundred thirty-eight (138) randomized to standard PTA.

One hundred ninety-nine (199) of the randomized subjects completed their 24-month follow-up visit at the time of this analysis. Of those, one hundred three (103) were part of the Covera™ Vascular Covered Stent group and ninety-six (96) were in the PTA group. The primary reasons for subjects discontinuing prior to the 24-month follow-up were withdrawal of consent (9), death (59), lost to follow-up (10), and discontinued due to other reasons (1).

Summary of Safety

Evaluation of the primary safety endpoint demonstrated statistical significance of non-inferiority of subjects randomized to Covera™ Vascular Covered Stent compared to subjects treated with PTA only. The proportion of subjects free from primary safety events was 95.0% in subjects treated with Covera™ Vascular Covered Stent compared with a safety rate of 96.4% in subjects treated with PTA alone (p-value = 0.0022), which confirms non-inferiority of the Covera™ Vascular Covered Stent with respect to the primary safety endpoint.

Table 27: Freedom from any Safety Event through 30 days (ITT Subjects), AVeNEW IDE

Primary Safety Endpoint	Covera™ Vascular Covered Stent n/N (%)	PTA n/N (%)	Difference 90% CI [2]	P-value [1]
Proportion Free from Primary Safety Events	133/140* (95.0)	132/137** (96.4)	-1.4 (-7.3, 4.6)	0.0022
Had Failure:	7/140 (5.0)	5/137 (3.6)		
Death	0	0		
Required Additional Intervention	7/140 (5.0)	5/137 (3.6)		
In-Patient Hospitalization or Prolongation	0	1/137 (0.7)		

*Two subjects were excluded from the analysis due to discontinuation or death prior to day 23 of their follow-up.

**One subject was excluded from the analysis due to death prior to day 23 of their follow-up.

[1] The p-value is calculated using Farrington and Manning non-inferiority test with non-inferiority margin=10%.

[2] 95% confidence interval is estimated using the Farrington and Manning method.

Note: The safety events are based on CEC adjudicated outcomes.

Tables 28 and 29 below show the rates of adverse events that were adjudicated to be definitely or possibly related to the study device and procedure at 30 days, 6, 12 and 24 months.

Table 28: CEC Adjudicated Device Related Adverse Events through 24 months (ITT Subjects), AVeNEW IDE

Adverse Event	Covera™ Vascular Covered Stent N=142				PTA Alone N=138			
System Organ Class/ Preferred Term	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)
Subjects with at Least One Device Related AEs	**12 (8.5%)**	**15 (10.6%)**	**17 (12.0%)**	**22 (15.5%)**	**1 0.7%)**	**2 (1.4%)**	**6 (4.3%)**	**10 (7.2%)**
Cardiac disorders	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
Bradycardia	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
General disorders and administration site conditions	1 (0.7%)	2 (1.4%)	2 (1.4%)	6 (4.2%)	0	0	0	1 (0.7%)
Death	0	0	0	4 (2.8%)	0	0	0	1 (0.7%)
Stent malfunction	0	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0
Vessel puncture site haemorrhage	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Infections and infestations	0	0	1 (0.7%)	1 (0.7%)	0	0	1 (0.7%)	2 (1.4%)
Arteriovenous fistula site infection	0	0	0	0	0	0	0	1 (0.7%)
Staphylococcal bacteraemia	0	0	1 (0.7%)	1 (0.7%)	0	0	1 (0.7%)	1 (0.7%)
Injury, poisoning and procedural complications	8 (5.6%)	8 (5.6%)	10 (7.0%)	11 (7.7%)	0	1 (0.7%)	3 (2.2%)	4 (2.9%)
Arteriovenous fistula site complication	5 (3.5%)	5 (3.5%)	8 (5.6%)	9 (6.3%)	0	1 (0.7%)	2 (1.4%)	2 (1.4%)
Arteriovenous fistula site haematoma	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Arteriovenous fistula site haemorrhage	0	0	0	0	0	0	0	1 (0.7%)
Procedural pain	2 (1.4%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0
Vascular pseudoaneurysm	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
Metabolism and nutrition disorders	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
Hyperkalaemia	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
Musculoskeletal and connective tissue disorders	1 (0.7%)	3 (2.1%)	3 (2.1%)	3 (2.1%)	0	0	0	0
Musculoskeletal pain	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Pain in extremity	1 (0.7%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0
Vascular disorders	2 (1.4%)	3 (2.1%)	3 (2.1%)	3 (2.1%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	2 (1.4%)
Steal syndrome	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	1 (0.7%)
Subclavian artery occlusion	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Vasospasm	2 (1.4%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.

Table 29: CEC Adjudicated Procedure Related Adverse Events through 24 months (ITT Subjects), AVeNEW IDE

Adverse Event	Covera™ Vascular Covered Stent (N=142)				PTA (N=138)			
System Organ Class/Preferred Term	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)
Subjects with at Least One Procedure Related AEs	13 (9.2%)	13 (9.2%)	13 (9.2%)	13 (9.2%)	8 (5.8%)	9 (6.5%)	10 (7.2%)	10 (7.2%)
Gastrointestinal disorders	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Abdominal pain lower	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
General disorders and administration site conditions	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Stent malfunction	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Vessel puncture site haemorrhage	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Injury, poisoning and procedural complications	9 (6.3%)	9 (6.3%)	9 (6.3%)	9 (6.3%)	1 (0.7%)	1 (0.7%)	2 (1.4%)	2 (1.4%)
Arteriovenous fistula site complication	5 (3.5%)	5 (3.5%)	5 (3.5%)	5 (3.5%)	0	0	0	0
Arteriovenous fistula site haematoma	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Contrast media reaction	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Procedural pain	2 (1.4%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0
Vascular procedure complication	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Vascular pseudoaneurysm	0	0	0	0	0	0	1 (0.7%)	1 (0.7%)
Musculoskeletal and connective tissue disorders	1 (0.7%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	0	0	0	0
Musculoskeletal pain	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Pain in extremity	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	0	0	0	0
Vascular disorders	2 (1.4%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	6 (4.3%)	7 (5.1%)	7 (5.1%)	7 (5.1%)
Flushing	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Steal syndrome	0	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)
Subclavian artery occlusion	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Vascular fragility	0	0	0	0	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)
Vascular rupture	0	0	0	0	3 (2.2%)	3 (2.2%)	3 (2.2%)	3 (2.2%)
Vasospasm	2 (1.4%)	2 (1.4%)	2 (1.4%)	2 (1.4%)	1 (0.7%)	1 (0.7%)	1 (0.7%)	1 (0.7%)

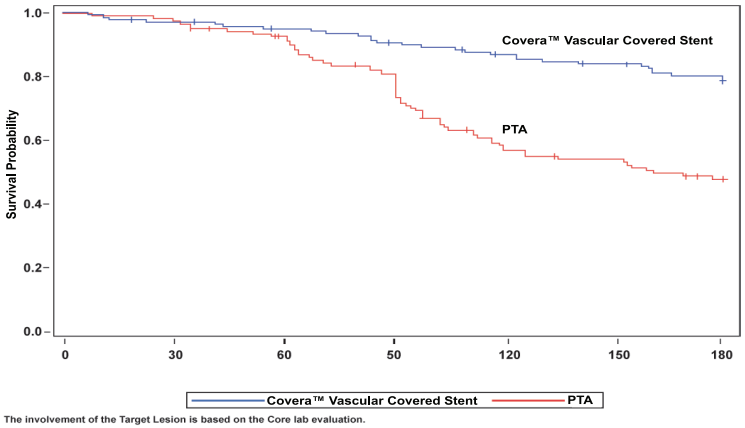
Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.

Summary of Effectiveness

The primary effectiveness endpoint is a measure based on TLPP at 6 months post-index procedure and was performed using the survival analysis method. The Kaplan-Meier estimates at day 180 for subjects receiving the Covera™ Vascular Covered Stent was 78.7% and for subjects receiving PTA alone was 47.9% (p-value <0.001). The primary effectiveness endpoint for superiority of Covera™ Vascular Covered Stent to PTA alone was met with a p-value of <0.001.

Table 30 below shows the TLPP rates in AV Fistula at 180 days, Table 31 shows TLPP rates for all reported timepoints through 6 months, and Figure 12 shows the Kaplan-Meier Analysis of TLPP at 180 days.

Figure 12: Kaplan-Meier Analysis of TLPP at 180 Days (mITT Subjects), AVeNEW IDE



The involvement of the Target Lesion is based on the Core lab evaluation.

Table 30: TLPP Rates in AV Fistula at 180 Days (mITT Subjects), AVeNEW IDE

Time Point	#of Subjects at Risk	#of Subjects Censored	#of Subjects with TLPP Fail	K-M Rate	(95% CI) [1]	Hazard Ratio [3] (95% CI)	P-value [2]
Covera™ Vascular Covered Stent	0	112	29	78.7	(70.8,84.7)	0.322 (0.207,0.503)	<0.001
PTA Alone	0	64	62	47.9	(38.7,56.6)		

[1] The rates are estimated using Kaplan-Meier method and the 95% confidence interval are estimated using Greenwood's formula.
[2] One sided P-value is calculated using Log-rank test.
[3] Hazard ratio calculated using COX regression with treatment in the model.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Table 31: TLPP Rates in AV Fistula at All Timepoints Through 6 Months (mITT Subjects), AVeNEW IDE

	Time Point (days)	#of Subjects at Risk	#of Subjects Censored	#of Subjects with TLPP Fail	K-M Rate	(95% CI) [1]	Hazard Ratio [3] (95% CI)	P-value [2]
Covera™ Vascular Covered Stent	30	136	1	4	97.2	(92.6,98.9)	0.322 (0.207,0.503)	<0.001
	90	124	4	13	90.6	(84.4,94.5)		
	180	0	112	29	78.7	(70.8,84.7)		
PTA Alone	30	122	1	3	97.6	(92.8,99.2)		
	90	97	6	23	81.1	(73.0,87.1)		
	180	0	64	62	47.9	(38.7,56.6)		

[1] The rates are estimated using Kaplan-Meier method and the 95% confidence interval are estimated using Greenwood's formula.
[2] One sided P-value is calculated using Log-rank test.
[3] Hazard ratio calculated using COX regression with treatment in the model.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Secondary Endpoints with Hypothesis Testing

Testing of secondary endpoints was performed in a hierarchical fashion in the order listed. Thus, in order to perform hypothesis test of ACPP at 6-month, TLPP at 12-months must be successful. The results of TLPP achieved statistical significance, indicating that it provides evidence that Covera™ Vascular Covered Stent is superior to PTA alone on this key secondary endpoint at 12 months.

Figure 13: Kaplan-Meier Analysis of TLPP at 365 Days (mITT Subjects), AVeNEW IDE

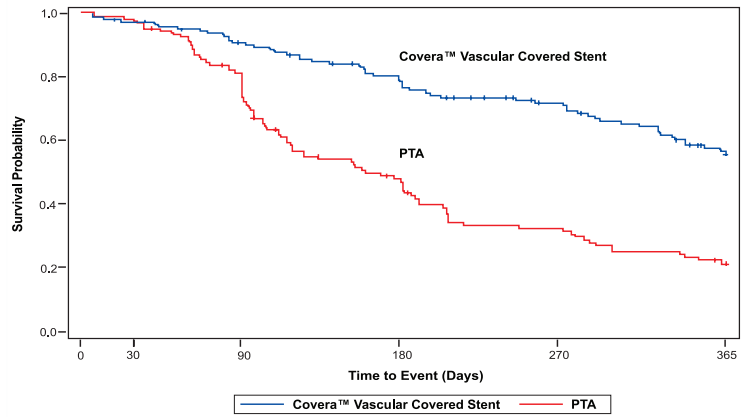


Table 32: TLPP Rates in AV Fistula at 365 Days (mITT Subjects), AVeNEW IDE

	Time Point (days)	#of Subjects at Risk	#of Subjects Censored	#of Subjects with TLPP Fail	K-M Rate	(95% C) [1]	Hazard Ratio [3] (95% CI)	P-value [2]
Covera™ Vascular Covered Stent	30	136	1	4	97.2	(92.6, 98.9)	0.348 (0.249,0.487)	<0.001
	90	124	4	13	90.6	(84.4, 94.5)		
	180	104	8	29	78.7	(70.8, 84.7)		
	365	0	84	57	55.8	(46.7,64.0)		
PTA Alone	30	122	1	3	97.6	(92.8, 99.2)		
	90	97	6	23	81.1	(73.0, 87.1)		
	180	53	11	62	47.9	(38.7, 56.6)		
	365	0	35	91	21.2	(14.2, 29.2)		

[1] The rates are estimated using Kaplan-Meier method and the 95% confidence interval are estimated using Greenwood's formula.
[2] One sided P-value is calculated using Log-rank test.
[3] Hazard ratio calculated using COX regression with treatment in the model.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

ACPP is defined as the interval following the index intervention until the next access thrombosis or clinically driven repeated intervention. A survival analysis of ACPP was performed by Kaplan-Meier estimates for 180 days. The results of ACPP did not meet statistical significance, indicating that is does not provide evidence that Covera™ Vascular Covered Stent is superior to PTA alone on this key secondary endpoint at 6 months.

Figure 14: Kaplan-Meier Analysis of ACPP at 180 days (mITT Subjects), AVeNEW IDE

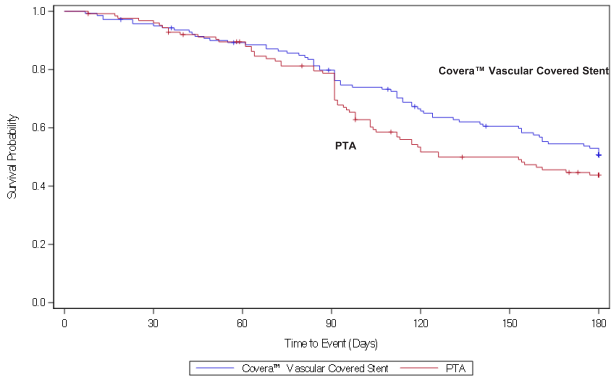


Table 33: Kaplan-Meier Analysis of ACPP through 180 days (mITT Subjects), AVeNEW IDE

	Time Point (days)	#of Subjects at Risk	#of Subjects Censored	#of Subjects with ACPP Fail	K-M Rate	(95% CI) [1]	Hazard Ratio [3] (95% CI)	P-value [2]
Covera™ Vascular Covered Stent	30	133	1	7	95.0	(89.8, 97.6)	0.787 (.560, 1.108)	0.0846
	90	109	4	28	79.8	(72.1, 85.6)		
	180	0	74	67	50.7	(42.0, 58.8)		
PTA Alone	30	120	1	5	96.0	(90.7, 98.3)		
	90	94	6	26	78.8	(70.4, 85.0)		
	180	0	59	67	43.8	(34.7, 52.5)		

[1] The rates are estimated using Kaplan-Meier method and the 95% confidence interval are estimated using Greenwood's formula.
[2] One sided P-value is calculated using Log-rank test.
[3] Hazard ratio calculated using COX regression with treatment in the model.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Subgroup Analysis

The primary effectiveness endpoint was evaluated by subgroup. Table 34 below shows the proportional analysis of TLPP at 6 months by subgroup. For all subgroups, the proportional analysis of TLPP for subjects in the Covera™ Vascular Covered Stent study arm was numerically greater than TLPP for subjects in the PTA only study arm. Additionally, Covera™ Vascular Covered Stent demonstrated effectiveness in all subgroups analyzed (p-value < 0.001).

Table 34: Analysis of TLPP at 6 Months by Subgroup (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
Target Lesion Characteristics		
de Novo	25/31 (80.6)	21/32 (65.6)
Re-stenotic	80/103 (77.7)	34/85 (40.0)
Target Lesion Location		
Cephalic Vein Arch	58/77 (75.3)	23/60 (38.3)
Cephalic Vein Outflow	18/22 (81.8)	12/18 (66.7)
Basilic Vein Outflow	9/11 (81.8)	6/14 (42.9)
Basilic Vein Swing-Point	13/15 (86.7)	9/15 (60.0)
Others	7/9 (77.8)	5/10 (50.0)
Presence of Secondary Lesion(s)?		
Yes	36/47 (76.6)	17/45 (37.8)
No	69/87 (79.3)	38/72 (52.8)
Fistula Configuration		
Radiocephalic	10/11 (90.9)	2/5 (40.0)
Transposed Brachiobasilic	21/25 (84.0)	18/34 (52.9)
Brachiocephalic	61/80 (76.3)	30/65 (46.2)
All Other	13/18 (72.2)	5/13 (38.5)

[1] The p-value is calculated using Cox regression with treatment, variable, and treatment by variable interaction.
[2] The 95% confidence interval is calculated using the exact binomial method.
n= number of subjects with TLPP event, N= number of subjects in the mITT Population with evaluable data.

Additional Endpoints

Tables 35-41 present information on additional endpoints with proportional values through 24 months.

Acute Technical Success is defined as successful deployment, based on the operator's opinion, of the implant to the intended location assessed at the time of the index procedure. Acute Procedure Success was defined as anatomic success and resolution of the pre-procedural clinical indicator(s) (clinical success) of a hemodynamically significant stenosis as further defined by Anatomic and Clinical Success. Anatomic Success was determined during the primary procedure and was defined as the achievement of a post-procedure residual stenosis of less than or equal to 30%, measured at the narrowest point of the lumen when compared to the adjacent non-stenosed venous segment. Whereas Clinical Success was defined as resolution of pre-procedural clinical indicators of access malfunction in the opinion of the investigator prior to hospital discharge which could include an abnormal physical exam, abnormal pressure monitoring parameters, decreased access flow, difficulty with dialysis needle puncture, pulling thrombus, prolonged bleeding, increased recirculation, and/or inadequate dialysis clearance.

Secondary Patency is defined as the interval after the index intervention until the access is abandoned. Multiple repetitive treatments can be included in post-intervention secondary patency

Table 35: TLPP, Proportional Value (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	136/140 (97.1%)	122/125 (97.6%)
90 days	125/138 (90.6%)	98/121 (81.0%)
6 months	105/134 (78.4%)	55/117 (47.0%)
12 months	67/124 (54.0%)	23/114 (20.2%)
18 months	44/116 (37.9%)	16/111 (14.4%)
24 months	40/114 (35.1%)	10/110 (9.1%)

Note N= number of subjects in the mITT population

Table 36: ACPP, Proportional Values (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	133/140 (95.0%)	120/125 (96.0%)
90 days	110/138 (79.7%)	95/121 (78.5%)
6 months	67/134 (50.0%)	50/117(42.7%)
12 months	33/128 (25.8%)	19/114 (16.7%)

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
18 months	17/122 (13.9%)	13/112(11.6%)
24 months	13/121 (10.7%)	9/111(8.1%)

Note N= number of subjects in the mITT population

Table 37: Additional Endpoints at Index Procedure, Proportional Values (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
Acute technical success	140/140 (100) [1]	--
Acute procedure success	138/140 (98.6)	124/126 (98.4%)

Note N= number of subjects in the mITT population
[1] One subject randomized to Covera™ Vascular Covered Stent was treated with PTA only; another subject that was randomized to Covera™ Vascular Covered Stent did not receive treatment at all.

Table 38: Secondary Patency, Proportional Values (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	139/140 (99.3)	125/125 (100.0)
90 days	136/138 (98.6)	119/120 (99.2)
6 months	131/134 (97.8)	113/115 (98.3)
12 months	115/123 (93.5)	102/105 (97.1)
18 months	103/112 (92.0)	91/94 (96.8)
24 months	95/104 (91.3)	76/82 (92.7)

Note N= number of subjects in the mITT population

Table 39: Proportion Free from Device and Procedure-Related AEs (ITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	127/140 (90.7)	132/137 (96.4)
90 days	124/138 (89.9)	127/133 (95.5)
6 months	118/134 (88.1)	122/129 (94.6)
12 months	108/126 (85.7)	112/123 (91.1)
18 months	99/120 (82.5)	102/114 (89.5)
24 months	91/114 (79.8)	90/104 (86.5)

Note that the relationships with device/procedure of the events are based on CEC adjudications.
Note N = number of subjects in the ITT population

The following tables present information on additional timepoints with total number and mean values through 24 months. Total Number of AV Access Circuit Reinterventions is defined as the number of reinterventions to the AV access circuit until access abandonment or through study completion. Total Number of Target Lesion Reinterventions is defined as the number of reinterventions to maintain target lesion patency.

Table 40: Total Number of AV Access Circuit Reinterventions (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent		PTA Alone	
	n	mean (SD)	n	mean (SD)
30 days	7	0.05 (0.219)	6	0.05 (0.215)
90 days	35	0.25 (0.528)	34	0.28 (0.609)
6 months	103	0.77 (0.933)	107	0.91 (0.970)
12 months	226	1.75 (1.479)	241	2.10 (1.606)
18 months	310	2.50 (2.062)	313	2.77 (2.022)
24 months	390	3.17 (2.645)	398	3.59 (2.560)

Table 41: Total Number of Target Lesion Reinterventions (mITT Subjects), AVeNEW IDE

Subgroup	Covera™ Vascular Covered Stent		PTA Alone	
	n	mean (SD)	n	mean (SD)
30 days	5	0.04 (0.186)	3	0.02 (0.154)
90 days	16	0.12 (0.385)	24	0.20 (0.442)
6 months	40	0.30 (0.615)	92	0.79 (0.850)
12 months	95	0.78 (0.992)	196	1.72 (1.340)
18 months	139	1.22 (1.239)	248	2.21 (1.652)
24 months	179	1.60 (1.579)	309	2.81 (2.025)

Tables 42 and 43 present information on the number of reinterventions at 24 months based on site reported and core lab adjudicated data, respectively. Table 44 presents information on the vessel and location of all AV access circuit reinterventions at 24 months.

Table 42: Number of Reinterventions at 24-months Based on Site Reported Data (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent		PTA Alone	
	N[1]	n[2]	N[1]	n[2]
Total Number of AV Access Interventions	112	396	107	401
Total Number of Target Lesion Interventions	68	155	102	293
Non-Target Lesion at Time of Index Procedure	33	103	27	77
New Lesion within the Access Circuit	89	235	66	174
Access Thrombosis	19	23	17	23

[1] N = number of subjects with at least one AV access circuit / target lesion intervention
[2] n = total number of AV access circuit / target lesion interventions
Reinterventions that occurred up to day 730 are included

Table 43: Number of Reinterventions at 24 months Based on Core Lab Adjudicated Data (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent		PTA Alone	
	N[1]	n[2]	N[1]	n[2]
Total Number of AV Access Interventions	110	374	105	385
Total Number of Target Lesion Interventions	76	179	103	309
Non-Target Lesion at Time of Index Procedure	31	96	26	75
New Lesion within the Access Circuit	76	195	59	146
Access Thrombosis	15	16	13	16

[1] N = number of subjects with at least one AV access circuit / target lesion intervention
[2] n = total number of AV access circuit / target lesion interventions
Reinterventions that occurred up to day 730 are included

Table 44: All Access Circuit Reinterventions at 24 months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
AV Access Circuit Re-interventions Performed?	396	401
Vessel		
Subclavian Vein	17 (4.3%)	8 (2.0%)
Axillary Vein	5 (1.3%)	7 (1.8%)
Brachial Vein	6 (1.5%)	3 (0.8%)
Cephalic Vein	211 (53.4%)	205 (51.3%)
Basilic Vein	75 (19.0%)	110 (27.5%)
Other	81 (20.5%)	67 (16.8%)
Location		
Anastomotic	11 (2.8%)	4 (1.0%)
Juxta-Anastomotic	28 (7.1%)	7 (1.8%)
Forearm Venous Outflow	1 (0.3%)	3 (0.8%)
Cannulation Zone	6 (1.5%)	4 (1.0%)
Cephalic Vein Arch	85 (21.5%)	115 (28.8%)
Cephalic Vein Outflow	49 (12.4%)	26 (6.5%)
Basilic Vein Swing Point	3 (0.8%)	33 (8.3%)
Basilic Vein Outflow	36 (9.1%)	43 (10.8%)
Axillary Vein	4 (1.0%)	4 (1.0%)
Subclavian Vein	17 (4.3%)	7 (1.8%)
Brachio Cephalic Vein	17 (4.3%)	4 (1.0%)
Superior Vena Cava (SVC)	1 (0.3%)	2 (0.5%)
Arterial Inflow	1 (0.3%)	1 (0.3%)
Other	136 (34.4%)	147 (36.8%)

Reinterventions were performed within the access circuit to treat target lesions, non-target lesions, new lesions, access thrombosis or for a combination of these factors. Considering all of these clinical factors for reintervention in the access circuit, subjects within the Covera™ Vascular Covered Stent arm had 235 reinterventions that included at least one new lesion and subjects in the PTA-only arm had 174 reinterventions that included at least one new lesion. Table 45 identifies the treatment that was performed during these reinterventions and treatment outcome for each study arm.

Table 45: Additional Endpoints at 24 months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
Total Number of AV Access Circuit Reinterventions Involving New Lesion	235	174
Total Number of Subjects with at least one Reintervention involving New Lesion	89	66
Treatment		
Standard PTA	233 (84.7%)	173 (77.9%)
Cutting/Scoring Balloon(s)	1 (0.4%)	0
Bare Metal Stent	14 (5.1%)	30 (13.5%)
Thrombectomy/Thrombolysis	14 (5.1%)	9 (4.1%)
Stent Graft	9 (3.3%)	8 (3.6%)
Surgical Revision	1 (0.4%)	1 (0.5%)
DCB	1 (0.4%)	0
Treatment, Other*	2 (0.7%)	1 (0.5%)
Reintervention Successful?		
Yes	229 (97.4%)	173 (99.4%)
No	6 (2.6%)	1 (0.6%)

[1] N = total number of treatments involving new lesions

* Other treatment includes: one thrombin injection for one subject in the Covera™ Vascular Covered Stent cohort, one procedure abandonment due to guidewire prolapse in the Covera™ Vascular Covered Stent cohort, and one thromboaspiration and embolectomy in the PTA cohort.

Table 46 presents Index of Patency Function (IPF), which is defined as the time from the index study procedure to study completion or access abandonment divided by the number of visits for a reintervention performed on the AV access circuit in order to maintain vascular access for hemodialysis. A visit is defined as one (1) procedural event, regardless of the number or type of interventions performed during the visit. The index procedure is counted as the first visit to ensure all subjects have a denominator of at least one. Index of Patency – Target Lesion (IPF-T) is defined as the time from the index study procedure to study completion or complete access abandonment divided by the number of visits for a reintervention performed at the target lesion in order to maintain vascular access for hemodialysis.

Table 46: Analysis of Index of Patency Function, Mean Values (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent mean (SD)	PTA Alone mean (SD)
Index of Patency Function (days)		
30 Days	29.22 (3.420)	29.28 (3.219)
90 Days	79.41 (20.511)	78.98 (20.770)
6 Months	126.06 (54.449)	116.11 (53.175)
12 Months	172.04 (108.690)	146.09 (89.723)
18 months	199.31 (145.278)	175.70 (125.145)
24 months	219.45 (178.916)	180.59 (135.216)
Index of Patency Function – Target Lesion (days)		
30 Days	29.44 (2.958)	29.64 (2.305)
90 Days	85.15 (15.349)	81.35 (18.243)
6 Months	156.32 (43.724)	121.75 (51.940)
12 Months	256.32 (115.626)	160.37 (87.504)
18 months	318.24 (179.651)	200.64 (130.055)
24 months	380.40 (249.548)	217.57 (158.373)

Summary of Deaths

There were a total of 59 deaths reported in the 24-month follow-up period – twenty-seven (27) subjects who were randomized to the Covera™ Vascular Covered Stent and thirty-two (32) subjects who were randomized to PTA only. The most prevalent primary cause of death can be classified as cardiac-related with twelve (12) total deaths in subjects randomized to

Covera™ Vascular Covered Stent and twelve (12) total death in subjects randomized to PTA only. Five (5) deaths were CEC-adjudicated to be possibly related to the study device. Four (4) of these deaths were in subjects who were randomized to the Covera™ Vascular Covered Stent and one (1) in subjects who were randomized to PTA only. All other deaths were CEC-adjudicated to be considered not related to the study device or index procedure.

SUMMARY OF 36-MONTH FOLLOW-UP RESULTS (AVENEW EXTENDED FOLLOW-UP OF IDE COHORT)

When the Covera™ Vascular Covered Stent was approved by FDA for use in the venous outflow of AV fistulae, FDA required that follow-up in the AVeNEW IDE study be extended from 24 months to 36 months to fulfill post-approval requirements. This AVeNEW Extended Follow-Up of IDE cohort was intended to further evaluate long-term performance of the Covera™ Vascular Covered Stent and to assess the long-term impact of the device on both target lesion and access circuit patency. Subjects were required to reconsent to participate in the extended follow-up cohort. As such, post-hoc analysis for the select sub-set of subjects was completed. A select number of sites and subjects decided to participate. Thus, data presented in this section are for the sub-set of reconsented subjects who participated in the extended follow-up of IDE cohort. Only 85 subjects of the original 280 in the AVeNEW IDE study participated in the AVeNEW Extended Follow-Up of IDE cohort. Of these 85 subjects, 43 had been randomized to Covera™ Vascular Covered Stent and 42 had been randomized to PTA only.

Results for these subjects from initial enrollment in the AVeNEW IDE through the 36-month follow-up of the AVeNEW Extended Follow-Up of IDE cohort are presented below.

Subject Demographics and Baseline Characteristics

Demographic and baseline characteristics for the ITT population are provided in Table 47 below. The majority of the subjects were white (68.2%) and male (57.6%). The mean age at the time of index procedure was 59.9 ± 11.69 years with no difference between the two treatments arms in regard to age. A summary of relevant medical risk factors as well as selected medical his-

tory background for the ITT population is provided in Table 48. The expected morbidities for this population were observed, with nearly all subjects being hypertensive (96.5%), 71.8% diabetic, and 67.1% with elevated cholesterol (dyslipidemia).

Comparison of demographics and risk factors between the AVeNEW Extended Follow-Up of IDE cohort and the overall AVeNEW IDE study populations reveals that the extension participants were on average slightly younger (59.9 years vs. 63.0 years) and had a greater BMI (50.6% of extension participants had a BMI ≥ 30 compared to 44.6% of participants in the overall study). There were also fewer smokers in the AVeNEW Extended Follow-Up of IDE cohort (34.1%) compared to the full AVeNEW IDE study population (44.3%).

Comparison of demographics and risk factors among the subjects who participated in the AVeNEW Extended Follow-Up of IDE cohort found no statistical differences noted between the two treatment arms for demographics or any of the relevant risk factors. Although there were no statistical differences noted, the rate of dyslipidemia in the AVeNEW Extended Follow-Up of IDE cohort trended in opposite directions for the two study arms compared to the full AVeNEW IDE study population. Specifically, the incidence of dyslipidemia increased from 66.9% to 74.4% in the Covera™ Vascular Covered Stent group while it decreased from 61.6% to 59.5% in the PTA-only group.

Table 47: Subject Demographics (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
Age Categories	**n (%)**	**n (%)**	**n (%)**
< 65 years	26 (60.5%)	24 (57.1%)	50 (58.8%)
≥ 65 and <75 years	12 (27.9%)	16 (38.1%)	28 (32.9%)
≥ 75 years	5 (11.6%)	2 (4.8%)	7 (8.2%)
Sex	**n (%)**	**n (%)**	**n (%)**
Male	26 (60.5%)	23 (54.8%)	49 (57.6%)
Female	17 (39.5%)	19 (45.2%)	36 (42.4%)
Ethnicity	**n (%)**	**n (%)**	**n (%)**
Hispanic or Latino	14 (32.6%)	14 (33.3%)	28 (32.9%)
Not Hispanic or Latino	29 (67.4%)	28 (66.7%)	57 (67.1%)
Race	**n (%)**	**n (%)**	**n (%)**
Asian	0	2 (4.8%)	2 (2.4%)
Black or African American	12 (27.9%)	12 (28.6%)	24 (28.2%)
White	31 (72.1%)	27 (64.3%)	58 (68.2%)
Other	0	1 (2.4%)	1 (1.2%)
BMI Categories	**n (%)**	**n (%)**	**n (%)**
<30	18 (41.9%)	24 (57.1%)	42 (49.4%)
≥30	25 (58.1%)	18 (42.9%)	43 (50.6%)

Table 48: Medical History (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
Risk Factor	**n (%)**	**n (%)**	**n (%)**
Subjects with at Least One Risk Factors	43 (100.0%)	41 (97.6%)	84 (98.8%)
Diabetes	31 (72.1%)	30 (71.4%)	61 (71.8%)
Type 1	3 (7.0%)	4 (9.5%)	7 (8.2%)
Type 2	28 (65.1%)	26 (61.9%)	54 (63.5%)
Dyslipidemia	32 (74.4%)	25 (59.5%)	57 (67.1%)
Hypertension	42 (97.7%)	40 (95.2%)	82 (96.5%)
Cigarette Smoking	14 (32.6%)	15 (35.7%)	29 (34.1%)
Current	1 (2.3%)	4 (9.5%)	5 (5.9%)
Former	13 (30.2%)	11 (26.2%)	24 (28.2%)
Cardiovascular Disease	**n (%)**	**n (%)**	**n (%)**
Subjects with at Least One Type of Cardiovascular Disease	26 (60.5%)	29 (69.0%)	55 (64.7%)
Congestive Heart Failure (CHF)	6 (14.0%)	14 (33.3%)	20 (23.5%)
NYHA Class I	0	1 (2.4%)	1 (1.2%)
NYHA Class II	1 (2.3%)	1 (2.4%)	2 (2.4%)
NYHA Class Unknown	5 (11.6%)	12 (28.6%)	17 (20.0%)
Stroke	6 (14.0%)	8 (19.0%)	14 (16.5%)
Coronary Artery Disease (CAD)	11 (25.6%)	16 (38.1%)	27 (31.8%)
Myocardial Infarction (MI)	4 (9.3%)	6 (14.3%)	10 (11.8%)
Transient Ischemic Attack (TIA)	2 (4.7%)	1 (2.4%)	3 (3.5%)
Valvular Heart Disease	3 (7.0%)	3 (7.1%)	6 (7.1%)
Aortic Disease	1 (2.3%)	1 (2.4%)	2 (2.4%)
Deep Vein Thrombosis (DVT)	1 (2.3%)	1 (2.4%)	2 (2.4%)
Peripheral Arterial/Vascular Disease (PAD) (PVD)	7 (16.3%)	8 (19.0%)	15 (17.6%)
Atrial Fibrillation (A-Fib)	6 (14.0%)	3 (7.1%)	9 (10.6%)
Other	7 (16.3%)	5 (11.9%)	12 (14.1%)
Other Disease	**n (%)**	**n (%)**	**n (%)**
Subjects with at Least One Type of Other Disease	42 (97.7%)	38 (90.5%)	80 (94.1%)
Bleeding Disorder	3 (7.0%)	0	3 (3.5%)
Cancer	4 (9.3%)	1 (2.4%)	5 (5.9%)
Steal Syndrome	1 (2.3%)	0	1 (1.2%)
Other	42 (97.7%)	38 (90.5%)	80 (94.1%)

A summary of characteristics of the AV access circuit as reported by sites is shown in Table 49. The majority of subjects had upper arm access in the left arm with inflow provided by the brachial artery and outflow through the cephalic vein. The type of fistula configuration was matched between the study arms with nearly two-thirds (62.4%) having brachiocephalic access, and an additional 18.8% having a transposed brachiocephalic fistula. Overall, 28.2% of the subjects had a vein transposed to facilitate the fistula configuration.

Table 49: Description of Access Circuit, AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
	n (%)	**n (%)**	**n (%)**
Target Limb			
Left Arm	33 (76.7%)	36 (85.7%)	69 (81.2%)
Right Arm	10 (23.3%)	6 (14.3%)	16 (18.8%)
Access Position			
Forearm	2 (4.7%)	2 (4.8%)	4 (4.7%)
Upper Arm	41 (95.3%)	40 (95.2%)	81 (95.3%)
Inflow Artery			
Brachial	41 (95.3%)	40 (95.2%)	81 (95.3%)
Radial	2 (4.7%)	2 (4.8%)	4 (4.7%)

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
	n (%)	n (%)	n (%)
Outflow Vein			
Axillary	1 (2.3%)	0	1 (1.2%)
Basilic	9 (20.9%)	10 (23.8%)	19 (22.4%)
Cephalic	33 (76.7%)	32 (76.2%)	65 (76.5%)
Fistula Configuration			
Brachiocephalic	27 (62.8%)	26 (61.9%)	53 (62.4%)
Radiocephalic	2 (4.7%)	2 (4.8%)	4 (4.7%)
Transposed Brachiobasilic	8 (18.6%)	8 (19.0%)	16 (18.8%)
All Other	6 (14.0%)	6 (14.3%)	12 (14.1%)
Transposed?			
Yes	12 (27.9%)	12 (28.6%)	24 (28.2%)
No	31 (72.1%)	30 (71.4%)	61 (71.8%)

Interventions within 30 days prior to the index procedure on the index AV access circuit are shown in Table 50. A total of three (3) interventions were performed in two (2) subjects (2.4%) in the index AV access circuit within 30 days of being enrolled in this study. Two (2) of these involved the target lesion and were comprised of PTA (2) and thrombolysis and/or thrombectomy (1). Both subjects were randomized to PTA Alone.

Table 50: Previous Index AV Access Circuit Interventions, AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
	n/N (%)	n/N (%)	n/N (%)
Number of Subjects Who Underwent Any Interventions of the AV Access Circuit within 30 Days Prior to the Index Procedure	0/43 (0%)	2/42 (4.8%)	2/85 (2.4%)
Number of Subjects Planning to Undergo Any Interventions of AV Access Circuit within 30 Days	0	0	0
Number of Previous Interventions	**n**	**n**	**n**
Number of Previous Interventions	0	3	3
Number of Subjects	0	2	2
Mean (SD)	N/A	1.5 (0.71)	1.5 (0.71)

Site-reported baseline target lesion characteristics are shown in Table 51 and Table 52. The majority of lesions (72.9%) were re-stenotic in nature and a majority of the anastomoses (77.6%) were at the cephalic vein, with the majority of stenoses located at the cephalic vein arch (61.2%).

The reference vessel diameter averaged 8.0 ± 0.92 mm, the target lesion length ranged from 2 to 80 mm, with a mean stenosis of 73.9 ± 12.34% by visual estimation.

Table 51: Target Lesion Characteristics (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
De Novo?	**n (%)**	**n (%)**	**n (%)**
Yes	10 (23.3%)	13 (31.0%)	23 (27.1%)
No	33 (76.7%)	29 (69.0%)	62 (72.9%)
Vessel	**n (%)**	**n (%)**	**n (%)**
Axillary Vein	1 (2.3%)	0	1 (1.2%)
Basilic Vein	8 (18.6%)	9 (21.4%)	17 (20.0%)
Cephalic Vein	34 (79.1%)	32 (76.2%)	66 (77.6%)
Other	0	1 (2.4%)	1 (1.2%)
Lesion Location	**n (%)**	**n (%)**	**n (%)**
Axillary Vein	1 (2.3%)	0	1 (1.2%)
Basilic Vein Outflow	2 (4.7%)	2 (4.8%)	4 (4.7%)
Basilic Vein Swing Point	5 (11.6%)	5 (11.9%)	10 (11.8%)
Cephalic Vein Arch	27 (62.8%)	25 (59.5%)	52 (61.2%)
Cephalic Vein Outflow	6 (14.0%)	6 (14.3%)	12 (14.1%)
Forearm Venous Outflow	1 (2.3%)	1 (2.4%)	2 (2.4%)
Other	1 (2.3%)	3 (7.1%)	4 (4.7%)

Table 52: Angiographic Target Lesion Characteristics (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
	Mean (SD)	Mean (SD)	Mean (SD)
Reference Vessel Diameter (mm)	8.0 (0.74)	8.0 (1.08)	8.0 (0.92)
Target Lesion Length (mm)	30.9 (18.09)	31.4 (15.69)	31.1 (16.85)
Target Lesion Stenosis (%)	73.0 (12.83)	74.8 (11.90)	73.9 (12.34)

Table 53: Summary of Study Device Details (As Treated Population), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)
Stent Graft Configuration	**n (%)**
Flared	23 (53.5%)
Straight	20 (46.5%)
Stent Graft Diameter	**n (%)**
8 mm	11 (25.6%)
9 mm	15 (34.9%)
10 mm	17 (39.5%)
Stent Graft Length	**n (%)**
30 mm	1 (2.3%)
40 mm	18 (41.9%)
60 mm	14 (32.6%)
80 mm	8 (18.6%)
100 mm	2 (4.7%)
Placement Configuration	**n (%)**
Single Stent Graft Only	43 (100%)
Was Placement Successful at intended site?	**n (%)**
Yes	43 (100%)

The protocol and IFU required pre-dilatation of the target lesion and successful effacement by the angioplasty balloon to meet the final eligibility criteria. Residual stenosis ranged from 0 to 75% where 15 subjects (17.6%) were reported to have unsuccessful pre-dilation (defined as a residual stenosis of >30%). Of which, 9 subjects (20.9%) were randomized to Covera™ Vascular Covered Stent post PTA and 6 subjects (14.3%) were randomized to PTA. A summary of pre-dilatation details is provided in Table 54.

Table 54: Target Lesion Pre-Dilatation, AVeNEW Extended Follow-Up of IDE Cohort of IDE Cohort

	Covera™ Vascular Covered Stent (N=43)	PTA Alone (N=42)	Total (N=85)
	Mean (SD)	Mean (SD)	Mean (SD)
Balloon Diameter (mm)	8.6 (1.03)	8.5 (1.25)	8.5 (1.14)
Balloon Length (mm)	49.8 (16.55)	49.5 (17.24)	49.6 (16.79)
Number of Balloon Inflations	1.4 (0.76)	1.4 (0.70)	1.4 (0.72)
Maximum Pressure of Balloon Inflation (atm)	22.7 (6.30)	22.5 (5.43)	22.6 (5.85)
Total Duration of Inflation (sec)	39.3 (28.57)	49.5 (50.81)	44.4 (41.16)
Residual Stenosis (%)	21.1 (19.15)	16.2 (15.62)	18.7 (17.57)

Subject Accountability

A total of 85 subjects (30.4%) were re-consented for the AVeNEW Extended Follow-Up cohort out of 280 that were randomized in the study. Forty-three (43) were randomized to Covera™ Vascular Covered Stent and 42 were randomized to PTA only. All subjects who re-consented completed the 36-month follow-up.

Summary of Safety

Tables 55 and 56 below show the rates of adverse events that were adjudicated to be definitely or possibly related to the study device and procedure at 30 days, 6, 12, 24, and 36 months.

Table 55: CEC Adjudicated Device Related Adverse Events through 36 months (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

Adverse Event	Covera™ Vascular Covered Stent (N=43)					PTA Alone (N=42)				
System Organ Class/ Preferred Term	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)
Subjects with at Least One Device Related AEs	**3 (7.0%)**	**5 (11.6%)**	**6 (14.0%)**	**6 (14.0%)**	**7 (16.3%)**	**0**	**1 (2.4%)**	**2 (4.8%)**	**3 (7.1%)**	**4 (9.5%)**
General disorders and administration site conditions	**0**	**1 (2.3%)**	**1 (2.3%)**	**1 (2.3%)**	**1 (2.3%)**	**0**	**0**	**0**	**0**	**0**
Stent malfunction	0	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0	0
Injury, poisoning and procedural complications	2 (4.7%)	2 (4.7%)	3 (7.0%)	3 (7.0%)	4 (9.3%)	0	1 (2.4%)	2 (4.8%)	3 (7.1%)	4 (9.5%)
Arteriovenous fistula aneurysm	0	0	0	0	0	0	0	0	0	0
Arteriovenous fistula site complication	0	0	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	1 (2.4%)	1 (2.4%)	1 (2.4%)	2 (4.8%)
Arteriovenous fistula site haemorrhage	0	0	0	0	0	0	0	0	1 (2.4%)	1 (2.4%)
Procedural pain	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	0	0	0	0
Vascular graft thrombosis	0	0	0	0	0	0	0	0	0	0
Vascular pseudoaneurysm	0	0	0	0	0	0	0	1 (2.4%)	1 (2.4%)	1 (2.4%)
Wound	0	0	0	0	1 (2.3%)	0	0	0	0	0
Musculoskeletal and connective tissue disorders	1 (2.3%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	0	0	0	0
Pain in extremity	1 (2.3%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	0	0	0	0

Note that n=subjects with at least one event.
Note that events were coded using MedDRA version 16.1.

Table 56: CEC Adjudicated Procedure Related Adverse Events through 36 months (ITT Subjects), AVeNEW Extended Follow-Up of IDE

Adverse Event	Covera™ Vascular Covered Stent (N=43)					PTA Alone (N=42)				
System Organ Class/Preferred Term	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)
Subjects with at Least One Procedure Related AEs	3 (7.0%)	3 (7.0%)	3 (7.0%)	3 (7.0%)	3 (7.0%)	2 (4.8%)	2 (4.8%)	3 (7.1%)	3 (7.1%)	3 (7.1%)
Injury, poisoning and procedural complications	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	0	1 (2.4%)	1 (2.4%)	1 (2.4%)
Procedural pain	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	2 (4.7%)	0	0	0	0	0
Vascular pseudoaneurysm	0	0	0	0	0	0	0	1 (2.4%)	1 (2.4%)	1 (2.4%)
Musculoskeletal and connective tissue disorders	**1 (2.3%)**	**1 (2.3%)**	**1 (2.3%)**	**1 (2.3%)**	**1 (2.3%)**	**0**	**0**	**0**	**0**	**0**
Pain in extremity	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	1 (2.3%)	0	0	0	0	0
Vascular disorders	**0**	**0**	**0**	**0**	**0**	**2 (4.8%)**	**2 (4.8%)**	**2 (4.8%)**	**2 (4.8%)**	**2 (4.8%)**

Adverse Event	Covera™ Vascular Covered Stent (N=43)					PTA Alone (N=42)				
System Organ Class/Preferred Term	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)	30 days n(%)	6 months n(%)	12 months n(%)	24 months n(%)	36 months n(%)
Flushing	0	0	0	0	0	1 (2.4%)	1 (2.4%)	1 (2.4%)	1 (2.4%)	1 (2.4%)
Vascular rupture	0	0	0	0	0	1 (2.4%)	1 (2.4%)	1 (2.4%)	1 (2.4%)	1 (2.4%)

Note that n=subjects with at least one event.

Note that events were coded using MedDRA version 16.1.

Summary of Effectiveness

Tables 57-62 present information on endpoints with proportional values through 36 months.

Table 57: TLPP, Proportional Values (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

Time Point	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	42/43 (97.7%)	39/39 (100.0%)
90 days	41/42 (97.6%)	33/39 (84.6%)
6 months	35/42 (83.3%)	17/39 (43.6%)
12 months	23/42 (54.8%)	8/39 (20.5%)
18 months	16/42 (38.1%)	6/38 (15.8%)
24 months	15/42 (35.7%)	5/38 (13.2%)
36 months	11/42 (26.2%)	5/38 (13.2%)

Note: N = number of subjects in the mITT population who entered the 36-month study extension with evaluable data.

Table 58: ACPP, Proportional Values (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

Time Point	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	39/43 (90.7%)	38/39 (97.4%)
90 days	32/42 (76.2%)	31/39 (79.5%)
6 months	17/42 (40.5%)	13/39 (33.3%)
12 months	6/42 (14.3%)	6/39 (15.4%)
18 months	4/42 (9.5%)	4/38 (10.5%)
24 months	3/42 (7.1%)	4/38 (10.5%)
36 months	1/42 (2.4%)	3/38 (7.9%)

Note: N = number of subjects in the mITT population who entered the 36-month study extension with evaluable data.

Secondary Patency is defined as the interval after the index intervention until the access is abandoned. Multiple repetitive treatments can be included in post-intervention secondary patency.

Table 59: Secondary Patency, Proportional Values (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

Time Point	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
30 days	43/43 (100.0%)	39/39 (100.0%)
90 days	42/42 (100.0%)	39/39 (100.0%)
6 months	42/42 (100.0%)	39/39 (100.0%)
12 months	41/42 (97.6%)	38/38 (100.0%)
18 months	41/42 (97.6%)	37/37 (100.0%)
24 months	40/41 (97.6%)	36/37 (97.3%)
36 months	37/41 (90.2%)	33/34 (97.1%)

Note: N = number of subjects in the mITT population who entered the 36-month study extension with evaluable data.

Table 60: Proportion Free from Device and Procedure-Related AEs (ITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

Time Point	Covera™ Vascular Covered Stent n/N (%)	PTA Alone
30 days	40/43 (93.0%)	41/42 (97.6%)
90 days	40/43 (93.0%)	41/42 (97.6%)
6 months	38/43 (88.4%)	40/42 (95.2%)
12 months	37/43 (86.0%)	39/42 (92.9%)
18 months	37/43 (86.0%)	39/42 (92.9%)
24 months	37/43 (86.0%)	38/42 (90.5%)
36 months	36/43 (83.7%)	37/42 (88.1%)

Note that the relationships with device/procedure of the events are based on CEC adjudications.

Note: N = number of subjects in the ITT population who entered the 36-month study extension with evaluable data.

The following tables present information on additional timepoints with total number and mean values through 36 months. Total Number of AV Access Circuit Reinterventions is defined as the number of reinterventions to the AV access circuit until access abandonment or through study completion. Total Number of Target Lesion Reinterventions is defined as the number of reinterventions to maintain target lesion patency.

Table 61: Total Number of AV Access Circuit Reinterventions (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent n/N (%)		PTA Alone n/N (%)	
Time Point	n	Mean (SD)	n	Mean (SD)
30 days	4	0.09 (0.294)	1	0.03 (0.160)
90 days	14	0.33 (0.650)	8	0.21 (0.409)
6 months	39	0.93 (0.997)	38	0.97 (0.811)
12 months	92	2.19 (1.435)	85	2.18 (1.211)
18 months	124	2.95 (1.860)	121	3.18 (1.784)
24 months	161	3.83 (2.326)	160	4.21 (2.384)
36 months	233	5.55 (3.704)	210	5.53 (3.439)

Table 62: Total Number of Target Lesion Reinterventions (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent n/N (%)		PTA Alone n/N (%)	
Time Point	**n**	**Mean (SD)**	**n**	**Mean (SD)**
30 days	2	0.05 (0.213)	0	0.00 (0.00)
90 days	3	0.07 (0.342)	6	0.15 (0.366)
6 months	11	0.26 (0.627)	31	0.79 (0.767)
12 months	32	0.78 (0.909)	67	1.72 (1.025)
18 months	53	1.29 (1.209)	95	2.50 (1.447)
24 months	76	1.85 (1.667)	124	3.26 (1.996)
36 months	124	3.02 (2.593)	156	4.11 (2.902)

Tables 63 and 64 present information on the number of reinterventions at 36 months based on site reported and core lab adjudicated data, respectively. Table 65 presents information on the vessel and location of all AV access circuit reinterventions at 36 months.

Table 63: Number of Reinterventions at 36 Months Based on Site Reported Data (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent		PTA Alone	
	N[1]	**n[2]**	**N[1]**	**n[2]**
Total Number of AV Access Circuit Re-interventions	41	243	37	217
Total Number of Target Lesion Re-interventions	32	117	35	158
Total Number of Non-target Lesion Re-interventions	11	45	11	41
Total Number of New Lesion Re-interventions	35	127	27	85
Total Number of Access Thrombosis Re-interventions	7	8	8	12

[1] N = number of subjects with at least one AV access circuit / target lesion intervention
[2] n = Total Number of AV access circuit / target lesion interventions.

Table 64: Number of Reinterventions at 36 Months Based on Core Lab Adjudicated Data (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent		PTA Alone	
	N[1]	**n[2]**	**N[1]**	**n[2]**
Total Number of AV Access Circuit Re-interventions	41	227	36	206
Total Number of Target Lesion Re-interventions	33	124	35	156
Total Number of Non-target Lesion Re-interventions	10	37	12	41
Total Number of New Lesion Re-interventions	34	119	25	78
Total Number of Access Thrombosis Re-interventions	6	6	7	8

[1] N = number of subjects with at least one AV access circuit / target lesion intervention
[2] n = Total Number of AV access circuit / target lesion interventions.

Table 65: All Access Circuit Reinterventions at 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
AV Access Circuit Re-interventions Performed	243	217
Vessel		
Subclavian Vein	7 (2.9%)	4 (1.8%)
Axillary Vein	1 (0.4%)	0
Brachial Vein	3 (1.2%)	1 (0.5%)
Cephalic Vein	139 (57.2%)	130 (59.9%)
Basilic Vein	49 (20.2%)	50 (23.0%)
Other	44 (18.1%)	32 (14.7%)
Location		
Anastomotic	4 (1.6%)	2 (0.9%)
Juxta-Anastomotic	21 (8.6%)	2 (0.9%)
Forearm Venous Outflow	1 (0.4%)	3 (1.4%)
Cannulation Zone	3 (1.2%)	2 (0.9%)
Cephalic Vein Arch	69 (28.4%)	65 (30.0%)
Cephalic Vein Outflow	23 (9.5%)	20 (9.2%)
Basilic Vein Swing Point	5 (2.1%)	17 (7.8%)
Basilic Vein Outflow	24 (9.9%)	23 (10.6%)
Axillary Vein	2 (0.8%)	0
Subclavian Vein	9 (3.7%)	4 (1.8%)
Brachio Cephalic Vein	8 (3.3%)	3 (1.4%)
Superior Vena Cava (SVC)	1 (0.4%)	0
Other	73 (30.0%)	76 (35.0%)

Reinterventions were performed within the access circuit to treat target lesions, non-target lesions, new lesions, access circuit thrombosis or for a combination of these factors. Considering all of these clinical factors for intervention in the access circuit, subjects within the Covera™ Vascular Covered Stent arm had 127 reinterventions that included at least one new lesion and subjects in the PTA-only arm had 85 reinterventions that included at least one new lesion. Table 66 identifies the treatment that was performed during reintervention and treatment outcome for each study arm.

Table 66: Additional Endpoints at 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent n/N (%)	PTA Alone n/N (%)
Total Number of Reinterventions Involving New Lesions	127	85
Total Number of Subjects with at least one Reintervention involving New Lesion	35	27
Treatment		
Standard PTA	127 (90.7%)	85 (75.9%)
Cutting/Scoring Balloon(s)	0	1 (0.9%)
Bare Metal Stent	4 (2.9%)	18 (16.1%)
Thrombectomy/Thrombolysis	5 (3.6%)	5 (4.5%)
Stent Graft	3 (2.1%)	1 (0.9%)
Surgical Revision	0	1 (0.9%)
Treatment, Other	1 (0.7%)	1 (0.9%)
Reintervention Successful?		
Yes	124 (97.6%)	85 (100%)
No	3 (2.4%)	0 (0.0%)

Table 67 presents Index of Patency Function (IPF), which is defined as the time from the index study procedure to study completion or access abandonment divided by the number of visits for a reintervention performed on the AV access circuit in order to maintain vascular access for hemodialysis. A visit is defined as one (1) procedural event, regardless of the number or type of interventions performed during the visit. The index procedure is counted as the first visit to ensure all subjects have a denominator of at least one. Index of Patency Function – Target Lesion (IPF-T) is defined as the time from the index study procedure to study completion or complete access abandonment divided by the number of visits for a reintervention performed at the target lesion in order to maintain vascular access for hemodialysis.

Table 67: Analysis of Index of Patency Function Mean Values (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent	PTA Alone
	Mean (SD)	Mean (SD)
Index of Patency Function (IPF)		
30 Days	28.60 (4.409)	29.62 (2.402)
90 Days	77.32 (21.881)	80.77 (18.408)
6 Months	118.00 (53.656)	109.62 (49.289)
12 Months	149.55 (95.451)	140.71 (84.039)
18 Months	183.69 (130.545)	163.23 (107.436)
24 Months	207.97 (165.060)	178.66 (124.085)
36 Months	235.61 (188.208)	228.43 (192.410)
Index of Patency Function at Target Lesion (IPF-T)		
30 Days	29.30 (3.196)	30.00 (0.000)
90 Days	87.50 (11.436)	83.08 (16.448)
6 Months	161.07 (40.175)	120.77 (51.267)
12 Months	256.69 (109.890)	160.51 (85.819)
18 Months	318.80 (171.790)	195.77 (130.106)
24 Months	383.40 (248.695)	225.41 (166.871)
36 Months	450.88 (350.736)	306.02 (263.448)

Summary of Deaths

No deaths after 730 days occurred among subjects who consented to participate in the AVeNEW Extended Follow-Up of IDE cohort.

Comparison of Study Cohorts: Full AVeNEW IDE Study vs. AVeNEW Extended Follow-Up of IDE Cohort (sub-group)

The AVeNEW Extended Follow-Up of IDE cohort was intended to further evaluate long-term performance of the Covera™ Vascular Covered Stent and to assess the long-term impact of the device on both target lesion and access circuit patency. A post-hoc analysis of target lesion and access circuit patency using the survival analysis method is presented below to compare the results from the 85 subjects who re-enrolled for participation in the AVeNEW Extended Follow-Up of IDE cohort to those of the original 280 subjects in the full AVeNEW IDE study. Comparison of treatment impact was accomplished by superimposing the Kaplan-Meier plots of the AVeNEW Extended Follow-Up of IDE cohort on those of the full AVeNEW IDE study.

TLPP for the full AVeNEW IDE through 24 months is presented in Figure 15 and Table 68. TLPP for the AVeNEW Extended Follow-Up of IDE cohort through 36 months is presented in Figure 15 and Table 69. In both Kaplan-Meier analyses, continued TLPP benefit of the Covera™ Vascular Covered Stent compared to PTA Alone was observed. At 24 months, however, a difference in Kaplan-Meier event rates for each treatment group across study cohorts was observed. Namely, TLPP at 24 months in the Covera™ Vascular Covered Stent arm decreased (40.0% in the full AVeNEW IDE study vs. 35.7% in the AVeNEW Extended Follow-Up of IDE cohort) but TLPP at 24 months in the PTA Alone arm increased (11.6% in the full AVeNEW IDE study vs. 15.0% in the AVeNEW Extended Follow-Up of IDE cohort).

Figure 15: Kaplan-Meier Analysis of TLPP through 24 and 36 Months (mITT Subjects)

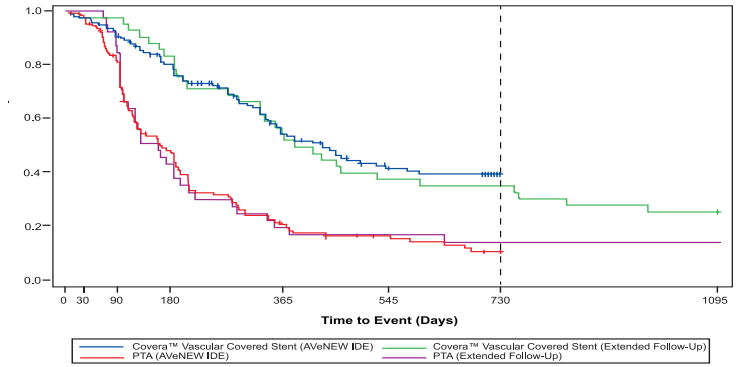


Table 68: Kaplan-Meier Analysis of TLPP through 24 Months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TLPP Failure	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TLPP Failure	K-M Rate[1]
30 Days	136	1	4	97.2	122	1	3	97.6
90 Days	124	4	13	90.6	97	6	23	81.1
180 Days	104	8	29	78.7	53	11	62	47.9
365 Days	63	21	57	55.8	22	13	91	21.2
545 Days	42	27	72	42.0	15	16	95	17.4
730 Days	0	67	74	40.0	0	26	100	11.6

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Table 69: Kaplan-Meier Analysis of TLPP through 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure TL Primary Patency	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure TL Primary Patency	K-M Rate[1]
30 Days	42	0	1	97.7	39	0	0	100.0
90 Days	41	1	1	97.7	33	0	6	84.6
180 Days	35	1	7	83.4	17	0	22	43.6
365 Days	23	1	19	54.8	8	0	31	20.5
545 Days	16	1	26	38.1	6	1	32	17.9

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure TL Primary Patency	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure TL Primary Patency	K-M Rate[1]
730 Days	15	1	27	35.7	5	1	33	15.0
1095 Days	0	12	31	26.2	0	6	33	15.0

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Freedom from Target Lesion Reinterventions for the full AVeNEW IDE through 24 months is presented in Figure 16 and Table 70. Freedom from Target Lesion Reinterventions for the AVeNEW Extended Follow-Up of IDE cohort through 36 months is presented in Figure 16 and Table 71. In both Kaplan-Meier analyses, continued TLPP benefit of the Covera™ Vascular Covered Stent compared to PTA Alone was observed. At 24 months, however, a difference in Kaplan-Meier event rates for each treatment group across study cohorts was observed. Namely, Freedom from Target Lesion Reinterventions at 24 months in the Covera™ Vascular Covered Stent arm decreased (38.4% in the full AVeNEW IDE study vs. 33.1% in the AVeNEW Extended Follow-Up of IDE cohort) but Freedom from Target Lesion Reinterventions at 24 months in the PTA Alone arm remained constant (9.5% in the full AVeNEW IDE study vs. 9.6% in the AVeNEW Extended Follow-Up of IDE cohort).

Figure 16: Freedom from Target Lesion Reinterventions through 24 and 36 Months (mITT Subjects)

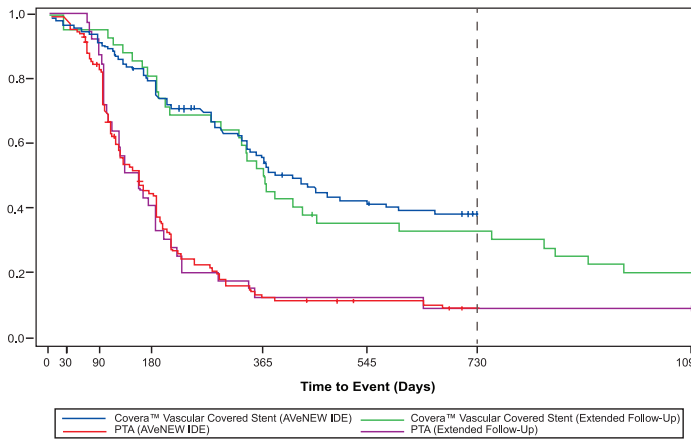


Table 70: Freedom from Target Lesion Reinterventions through 24 Months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TL reintervention	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TL reintervention	K-M Rate[1]
30 Days	135	1	5	96.4	122	1	3	97.6
90 Days	123	5	13	90.6	97	7	22	81.9
180 Days	102	9	30	77.9	48	12	66	44.0
365 Days	61	22	58	54.8	14	12	100	12.8
545 Days	39	30	72	41.6	10	15	101	11.9
730 Days	0	66	75	38.4	0	23	103	9.5

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Table 71: Freedom from Target Lesion Reinterventions through 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TL reintervention	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with TL reintervention	K-M Rate[1]
30 Days	41	0	2	95.3	39	0	0	100.0
90 Days	40	1	2	95.3	33	0	6	84.6
180 Days	34	1	8	81.0	16	0	23	41.0
365 Days	21	1	21	50.1	5	0	34	12.8
545 Days	14	2	27	35.6	4	1	34	12.8
730 Days	13	2	28	33.1	3	1	35	9.6
1095 Days	0	10	33	20.3	0	4	35	9.6

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

ACPP for the full AVeNEW IDE through 24 months is presented in Figure 17 and Table 72. ACPP for the AVeNEW Extended Follow-Up of IDE cohort through 36 months is presented in Figure 17 and Table 73. In both Kaplan-Meier analyses, diminishing ACPP benefit of the Covera™ Vascular Covered Stent over time compared to PTA Alone was observed. Differences in Kaplan-Meier event rates for each treatment group across study cohorts were, however, observed as early as at 12 months post-Index procedure. At 12 months, ACPP in the Covera™ Vascular Covered Stent arm decreased nearly 6 times more than in the PTA Alone arm in the AVeNEW Extended Follow-Up of IDE cohort when compared to the full AVeNEW IDE study (13.7% drop in the Covera™ Vascular Covered Stent arm vs. 2.3% drop in the PTA Alone arm). Additionally, at 24 months ACPP in the Covera™ Vascular Covered Stent arm decreased (14.6% in the full AVeNEW IDE study vs. 7.2% in the AVeNEW Extended Follow-Up of IDE cohort) but ACPP at 24 months in the PTA Alone arm increased (10.5% in the full AVeNEW IDE study vs. 12.8% in the AVeNEW Extended Follow-Up of IDE cohort).

Figure 17: Kaplan-Meier Analysis of ACPP through 24 and 36 Months (mITT Subjects)

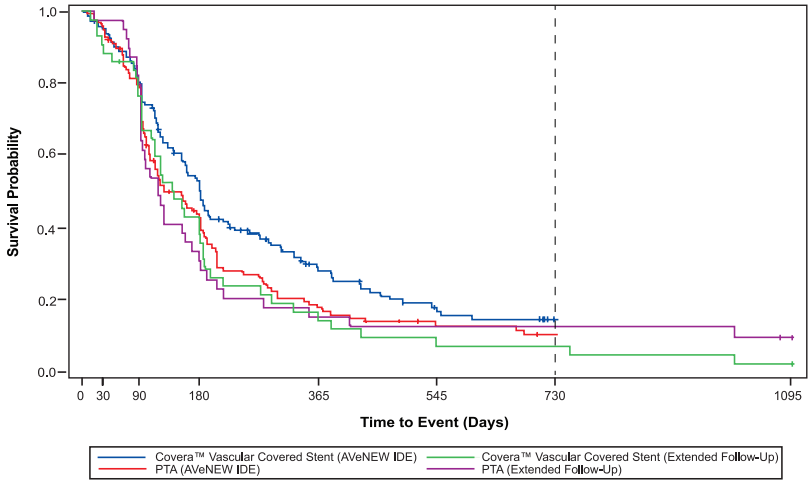


Table 72: Kaplan-Meier Analysis of ACPP through 24 Months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with ACPP Failure	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with ACPP Failure	K-M Rate[1]
30 Days	133	1	7	95.0	120	1	5	96.0
90 Days	109	4	28	79.8	94	6	26	78.8
180 Days	67	7	67	50.7	48	11	67	43.8
365 Days	29	17	95	28.0	19	12	95	17.7
545 Days	16	20	105	18.0	12	15	99	14.0
730 Days	0	33	108	14.6	0	24	102	10.5

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Table 73: Kaplan-Meier Analysis of ACPP through 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure AV Access Circuit Primary Patency	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with Failure AV Access Circuit Primary Patency	K-M Rate[1]
30 Days	39	0	4	90.7	38	0	1	97.4
90 Days	32	1	10	76.5	31	0	8	79.5
180 Days	17	1	25	40.6	13	0	26	33.3
365 Days	6	1	36	14.3	6	0	33	15.4
545 Days	4	1	38	9.6	4	1	34	12.8
730 Days	3	1	39	7.2	4	1	34	12.8
1095 Days	0	2	41	2.4	0	4	35	9.6

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Freedom from Access Circuit Reinterventions for the full AVeNEW IDE through 24 months is presented in Figure 18 and Table 74. Freedom from Access Circuit Reinterventions for the AVeNEW Extended Follow-Up of IDE cohort through 36 months is presented in Figure 18 and Table 75. In both Kaplan-Meier analyses, diminishing ACPP benefit of the Covera™ Vascular Covered Stent over time compared to PTA Alone was observed. Differences in Kaplan-Meier event rates for each treatment group across study cohorts were, however, observed as early as at 12 months post-Index procedure. At 12 months, Freedom from Access Circuit Reinterventions in the Covera™ Vascular Covered Stent arm decreased nearly 7 times more than in the PTA Alone arm in the AVeNEW Extended Follow-Up of IDE cohort when compared to the full AVeNEW IDE study (11.1% drop in the Covera™ Vascular Covered Stent arm vs. 1.6% drop in the PTA Alone arm). Additionally, at 24 months Freedom from Access Circuit Reinterventions in the Covera™ Vascular Covered Stent arm fell by half (14.0% in the full AVeNEW IDE study vs. 7.2% in the AVeNEW Extended Follow-Up of IDE cohort) but Freedom from Target Lesion Reinterventions at 24 months in the PTA Alone arm fell by only one-eighth (8.8% in the full AVeNEW IDE study vs. 7.7% in the AVeNEW Extended Follow-Up of IDE cohort).

Figure 18: Freedom from Access Circuit Reinterventions through 24 and 36 Months (mITT Subjects)

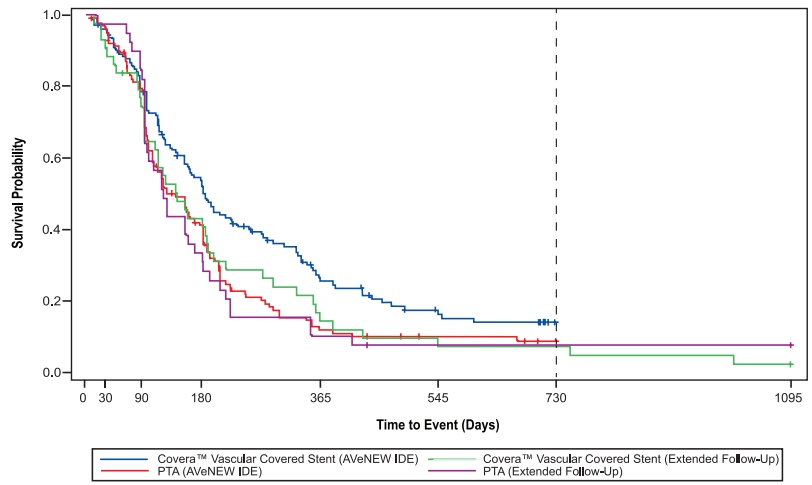


Table 74: Freedom from Access Circuit Reinterventions through 24 Months (mITT Subjects), AVeNEW IDE

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with AV Access Re-intervention	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with AV Access Re-intervention	K-M Rate[1]
30 Days	133	1	7	95.0	120	1	5	96.0
90 Days	107	4	30	78.4	94	6	26	78.8
180 Days	69	7	65	52.3	45	11	70	41.1
365 Days	27	16	98	25.5	13	11	102	11.9
545 Days	15	20	106	17.5	8	14	104	10.1
730 Days	0	32	109	14.0	0	21	105	8.8

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

Table 75: Freedom from Access Circuit Reinterventions through 36 Months (mITT Subjects), AVeNEW Extended Follow-Up of IDE Cohort

	Covera™ Vascular Covered Stent				PTA Alone			
Time Point	# of Subjects at Risk	# of Subjects Censored	# of Subjects with AV Access Re-intervention	K-M Rate[1]	# of Subjects at Risk	# of Subjects Censored	# of Subjects with AV Access Re-intervention	K-M Rate[1]
30 Days	39	0	4	90.7	38	0	1	97.4
90 Days	31	1	11	74.2	32	0	7	82.1
180 Days	18	1	24	43.1	13	0	26	33.3
365 Days	6	1	36	14.4	4	0	35	10.3
545 Days	4	1	38	9.6	2	1	36	7.7
730 Days	3	1	39	7.2	2	1	36	7.7
1095 Days	0	2	41	2.4	0	3	36	7.7

[1] The rates are estimated using Kaplan-Meier method.

Note: The involvement of the target lesion is based on the core lab evaluation. If images were not evaluable by the core lab, site reported evaluation was used.

The results of these comparisons show that patients randomized to the Covera™ Vascular Covered Stent arm who experienced worse outcomes at 24 months were more likely to participate in the AVeNEW Extended Follow-Up of IDE cohort. Additionally, these comparisons show that this tendency is not present in the PTA Alone arm. Indeed, patients randomized to the PTA Alone arm who experienced better outcomes at 24 months were actually slightly more likely to participate in the AVeNEW Extended Follow-Up of IDE cohort.

Due to the small sample size, different baseline characteristic profiles of the AVeNEW Extended Follow-Up of IDE cohort compared to the full AVeNEW IDE study, different patterns of Kaplan-Meier curves between the AVeNEW Follow-Up of IDE cohort compared to the full AVeNEW IDE study demonstrated in the analysis above, and the inherent survivorship bias, the results from the AVeNEW Extended Follow-Up of IDE cohort may not be generalizable to the larger patient population studied in the AVeNEW IDE study. TLPP continued to perform well through 36 months while ACPP was comparable between the Covera™ Vascular Covered Stent and PTA Alone groups, with no new concerns related to safety or efficacy.

Conclusions Drawn from the Study

The Covera™ Vascular Covered Stent was evaluated in the prospective, multi-center, randomized, concurrently-controlled AVeNEW clinical study designed to assess the safety and effectiveness of the Covera™ Vascular Covered Stent for the treatment of stenotic lesions in the upper extremity venous outflow of the AV access circuit of hemodialysis subjects dialyzing with an AV fistula.

The proportion of subjects free from primary safety events was 95.0% in subjects treated with Covera™ Vascular Covered Stent compared with a safety rate of 96.4% in subjects treated with PTA alone (p-value = 0.0022), which confirms non-inferiority of the Covera™ Vascular Covered Stent with respect to the primary safety endpoint.

The Kaplan-Meier estimates at day 180 for subjects receiving the Covera™ Vascular Covered Stent was 78.7% and for subjects receiving PTA alone was 47.9% (p-value <0.001). The primary effectiveness endpoint for superiority of Covera™ Vascular Covered Stent to PTA alone was met with a p-value of <0.001.

The study met the first key secondary endpoint of TLPP at 12 months (TLPP was 55.8% for Covera™ Vascular Covered Stent treated subjects, versus 21.2% in the PTA group) but it did not meet its second key secondary endpoint, ACPP at 6 months (ACPP was 50.7% for Covera™ Vascular Covered Stent treated subjects, versus 43.8% in the PTA group, p-value = 0.0846). Continued TLPP benefit of the Covera™ Vascular Covered Stent was observed using the proportional method through 24-months. ACPP results were comparable between the Covera™ Vascular Covered Stent and PTA Alone study arms, with no concerns related to safety or efficacy.

While the total number of reinterventions for access circuit were similar, there was a considerable reduction in the number of reinterventions for the target lesions after treatment with Covera™ Vascular Covered Stent compared to PTA alone. However, more reinterventions for new lesions in the access circuit were required in the Covera™ Vascular Covered Stent treated group (76 subjects had 195 reinterventions) compared to the PTA alone group (59 subjects had 146 reinterventions). The incidence of access thrombosis after treatment with the Covera™ Vascular Covered Stent was comparable to the incidence of access thrombosis following treatment with PTA only. Additionally, the incidence of secondary patency failure was consistent across both treatment groups. To preserve AV access, physicians should follow their site standard of care.

To assess the long-term benefit of the Covera™ Vascular Covered Stent, a post-hoc analysis was completed for the AVeNEW Extended Follow-Up cohort. A small sub-set of subjects in the AVeNEW IDE study were followed through 36-months. Due to the small sample size and different baseline characteristic profiles of the AVeNEW Extended Follow-Up of IDE cohort compared to the full AVeNEW IDE study, different patterns of Kaplan-Meier curves between the AVeNEW Extended Follow-Up of IDE cohort compared to the full AVeNEW IDE study, and the inherent survivorship bias, the results from the AVeNEW Extended Follow-Up of IDE cohort may not be generalizable to the larger patient population studied in the AVeNEW IDE study. TLPP continued to perform well through 36 months while ACPP was comparable between the Covera™ Vascular Covered Stent and PTA Alone groups, with no new concerns related to safety or efficacy.

Data from the clinical trial provide a reasonable assurance that the Covera™ Vascular Covered Stent is safe and effective when used for the treatment of stenoses in the venous outflow of an arterio-venous (AV) fistula.

Warranty

Bard Peripheral Vascular, Inc. warrants to the first purchaser of this product that this product will be free from defects in materials and workmanship for a period of one year from the date of first purchase and liability under this limited product warranty will be limited to repair or replacement of the defective product, in Bard Peripheral Vascular Inc.'s sole discretion or refunding your net price paid. Wear and tear from normal use or defects resulting from misuse of this product are not covered by this limited warranty.

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Some states/countries do not allow an exclusion of implied warranties, incidental or consequential damages. You may be entitled to additional remedies under the laws of your state/country.

Symbols used on Labeling

Rx Only — CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician

Consult Instructions For Use

Keep Away From Sunlight

Keep Dry

Do Not Use If Package Is Damaged

Single Use

Do Not Resterilize

Contents: (1)

MR Conditional

Not Made With Natural Rubber Latex

Non-Pyrogenic

REF — Catalogue Number

LOT — Lot Number

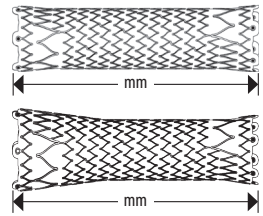
STERILE EO — Sterilized Using Ethylene Oxide

Use By

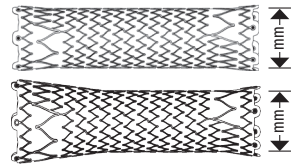
Manufacturer

Minimum Introducer Size

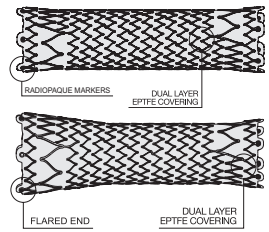
Guidewire Compatibility



Length



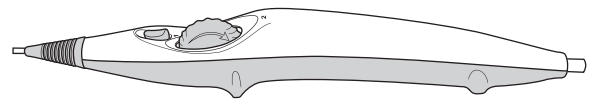
Diameter



Radiopaque Markers

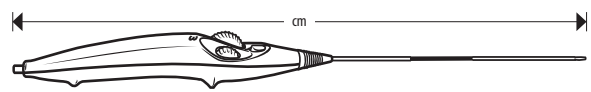
Dual Layer ePTFE Covering

Flared End



Triaxial Delivery System

Working Length



System Length

Labeling issue date: 2022-04

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