DE NOVO CLASSIFICATION REQUEST FOR EVERLINQ® ENDOAVF SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Percutaneous catheter for creation of an arteriovenous fistula for hemodialysis access. This device is a single use percutaneous catheter system that creates an arteriovenous fistula (AVF) in the arm of patients with chronic kidney disease who need hemodialysis.

NEW REGULATION NUMBER: 21 CFR 870.1252

CLASSIFICATION: II

PRODUCT CODE: PQK

BACKGROUND

DEVICE NAME: everlinQ® endoAVF System

SUBMISSION NUMBER: DEN160006

DATE OF DE NOVO: February 3, 2016

CONTACT: TVA Medical, Inc.
7000 Bee Cave Rd., Suite 250
Austin, TX 78746

INDICATIONS FOR USE

The everlinQ® endoAVF System is indicated for the creation of an arteriovenous fistula (AVF) using the ulnar artery and ulnar vein in patients with minimum artery and vein diameters of 2.0 mm and less than 2.0 mm separation between the artery and vein at the fistula creation site who have chronic kidney disease and need hemodialysis.

LIMITATIONS

The sale, distribution, and use of the everlinQ® endoAVF System are restricted to prescription use in accordance with 21 CFR 801.109.

Only physicians trained and experienced in endovascular techniques, who have received appropriate training with the device, should use the device. Endovascular technique training and experience should include ultrasound vessel access in the arm, guidewire navigation, radiographic imaging, embolization coil placement, and access closure.

The everlinQ® endoAVF System is contraindicated for patients with a distance between target artery and vein > 2mm, and patients with target vessels < 2mm in diameter.

The TVA Medical everlinQ® System is only to be used with the components specified in the labeling. Do not attempt to substitute a non-approved component or to use any component of this system with any other medical device system. Use of the system with other components, such as braided sheaths, may interfere with proper functioning of the device.

The 6F everlinQ System has only been evaluated for the creation of an AVF using the ulnar artery and ulnar vein. The device should not be used in place of a more distal AVF.

Adjunctive procedures are expected to be required at the time of the index procedure to increase and direct blood flow into the AVF target outflow vein to assist maturation. Care should be taken to proactively plan for any adjunctive procedures, such as embolization coil placement, when using the device.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The everlinQ® endoAVF System (everlinQ®) consists of two single-use disposable magnetic catheters: a venous catheter and an arterial catheter, both of which are 6 Fr in diameter. The venous catheter contains an electrode for delivery of radiofrequency (RF) energy while the arterial catheter contains a ceramic backstop that serves as a mechanical stop for the electrode. The everlinQ® is used with a commercially available electrosurgical unit (ESU) and electrosurgical pencil.

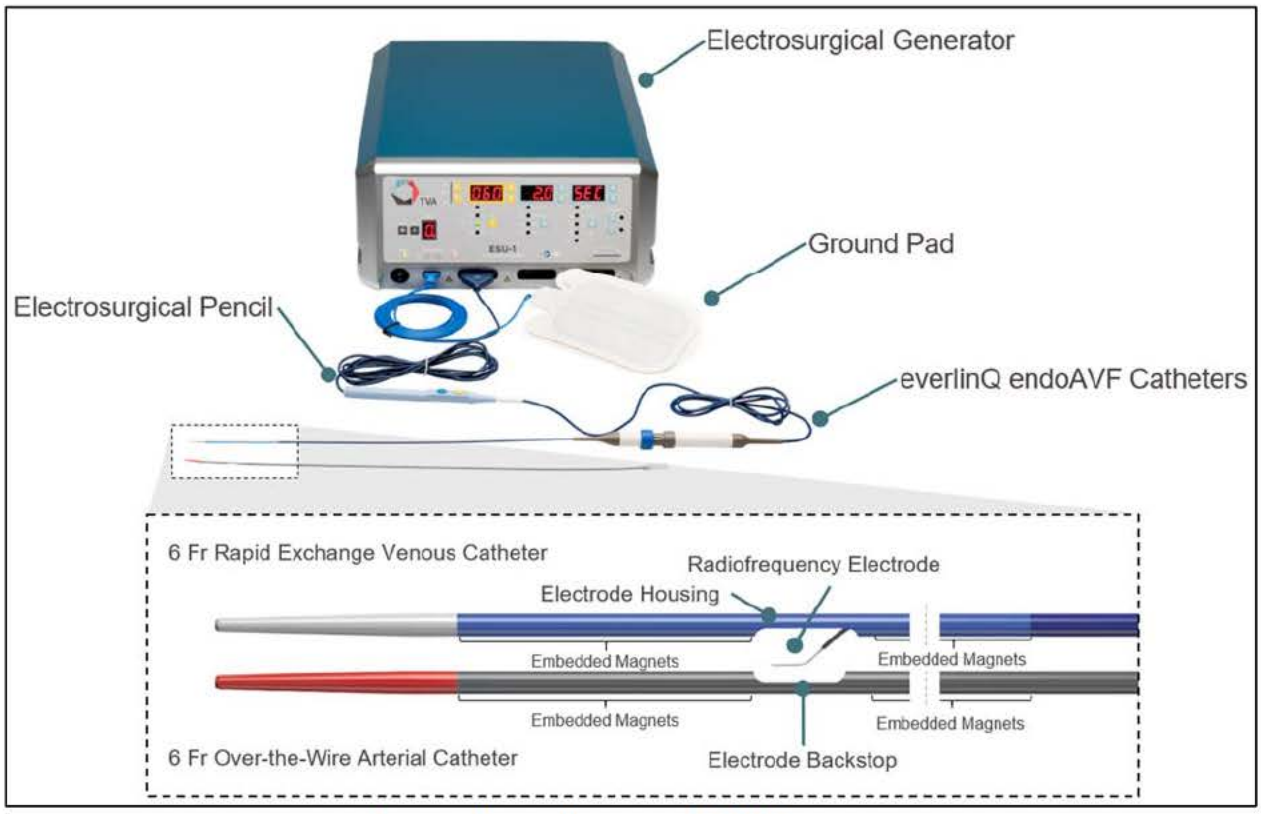


Figure 1: everlinQ® endoAVF System

The venous and arterial catheters are inserted into the ulnar vein and ulnar artery, respectively. The two catheters are then aligned and rotated, and when they achieve the proper position, the magnets contained in each catheter attract to one another, approximating the vessels while simultaneously aligning the electrode with the backstop. Using the ESU, grounding pad, and electrosurgical pencil, RF energy can then be delivered through the electrode for tissue cutting. This energy creates a small, rectangular hole (approximately 5 mm x 1 mm) in the adjoining vessels, allowing blood to flow from the artery to the vein and thereby creating a nonsurgical, or endovascular, arteriovenous fistula (endoAVF).

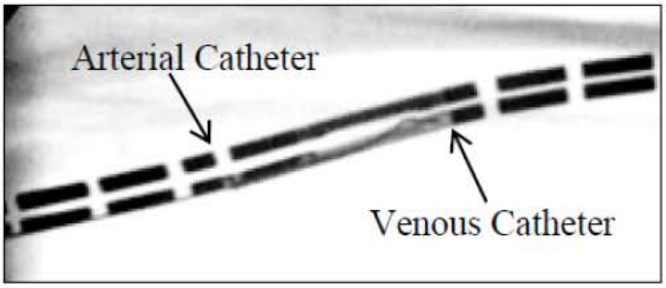


Figure 2: Proper alignment of the catheters

Please refer to the Instructions for Use for additional details.

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

The everlinQ® endoAVF System is an externally communicating device in contact with circulating blood with limited contact duration (< 24 hours). The biocompatibility testing summarized below was performed to demonstrate that the device is biocompatible for its intended use. All tests passed.

Table 1: Biocompatibility Testing Summary

Test	Description (Method)
Cytotoxicity	MEM Elution Assay with L-929 Mouse Fibroblast Cells (ISO 10993-5)
Sensitization	Guinea Pig Maximization (ISO 10993-10)
Irritation	Intracutaneous Reactivity (ISO 10993-10)
Acute System Toxicity	Acute Systemic Injection (ISO 10993-11)
Hemocompatibility	ASTM Hemolysis Assay – Direct Contact & Extract Methods (ASTM Method F756-08)
	Complement Activation C3a and SC5b-9 Determination of SC5b-9 Terminal Chain Complex (TCC) and C3a-desArg Present in Normal Human Serum Through Enzyme Immunoassay (ISO 10993-4)
	In-vivo Thromboresistance (evaluated as part of the animal studies)
Pyrogenicity	Material-mediated Rabbit Pyrogen (USP Rabbit Pyrogen Test Procedure, Section 151)
	Endotoxin-mediated (LAL) (AAMI ST72)

SHELF LIFE/STERILITY

The shelf-life of the everlinQ® endoAVF System has been established at 1 year based on accelerated aging testing equivalent to 1 year (13 months) in accordance with *ASTM F1980 - 07 Standard Guide for Accelerated Aging of Sterile Barrier Systems for Medical Devices*. Following 2X sterilization, environmental conditioning per ISTA 2A, distribution simulation per ASTM D4169, and accelerated aging, the devices were visually inspected for damage, bubble leak tested per ASTM F2096, and package seals were tested per ASTM F88. Aged devices also underwent repeat engineering bench testing to confirm acceptable performance.

The everlinQ® endoAVF System is labeled as sterile and has a validated sterility assurance level (SAL) of 10^{-6}. The everlinQ® endoAVF System has been validated to be sterilized via ethylene oxide (EO). The sterilization cycle was validated using the half cycle method per ISO 11135-1:2007, and the EO and ECH residuals were shown to meet the limits specified by ISO 10993-7:2008.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The electromagnetic compatibility and electrical safety of the everlinQ® endoAVF System was evaluated by demonstrating compliance to the following standards:

Table 2: Electrical Performance Testing Summary

Standard	Name
AAMI / ANSI ES60601-1:2005/(R)2012 and A1:2012, C1:2009/(R)2012 and A2:2010/(R)2012	Medical Electrical Equipment - Part 1: General Requirements For Basic Safety And Essential Performance
IEC 60601-1-2:2014	Medical Electrical Equipment - Part 1-2: General Requirements For Basic Safety And Essential Performance - Collateral Standard: Electromagnetic Disturbances - Requirements and Tests
IEC 60601-2-2:2009	Medical Electrical Equipment – Part 2-2: Particular Requirements For The Basic Safety And Essential Performance of High Frequency Surgery Equipment And High Frequency Surgical Accessories

MAGNETIC RESONANCE (MR) COMPATIBILITY

The everlinQ® endoAVF System is intended as a temporary use device and has not been tested for MR compatibility.

SOFTWARE

The everlinQ® endoAVF System does not contain software. The device is intended to be used with a commercially available ESU, electrosurgical pencil, and grounding pad.

PERFORMANCE TESTING – BENCH

The everlinQ® endoAVF System was subjected to a series of bench tests to assess its functional performance. These tests were performed on final, sterilized product. The engineering bench testing summarized in Table 3 below was performed to demonstrate acceptable mechanical performance of the device for its intended use.

Table 3: Performance Testing (Bench) Summary

Test		Description/Acceptance Criteria
Dimensional Verification	Electrode Wire Deployment (Distance)	The distance from distal tip of electrode (toe) to catheter shaft must measure .093" ± .010" when slide collar/electrode are in "fire" position.
	Electrode Wire Deployment (Angle)	Angle between flattened surface of the electrode and the centerline of the catheter shaft must measure 7.5° ± 2.5° when slide collar/electrode are in "fire" position.
Simulated Use	Simulated Use Conditioning	Track the device through a simulated worst-case anatomic model using the appropriate accessories (e.g. introducer sheaths).
	Handle Actuation	Electrodes must deploy from electrode housing when slide collar is pulled proximal to device and reside in "fire" position. Rotating slide lock must permit electrode to be pulled into the proximal electrode housing such that no part of the electrode protrudes no further than the outside diameter of the catheter.
	Device Alignment	With catheters magnetically apposed and electrode deployed, rotational and axial alignment must be held such that the electrode maintains contact within the margins of the arterial backstop in 100% of samples tested.
	Energy Delivery	Upon application of energy, devices must create heat eddies at the active electrode while exhibiting no degradation in insulative materials near the active electrode. The test also evaluated the ability of the device to deliver energy properly when used with the labeled electrosurgical generator.
	Tissue Cutting Test	Electrodes must be able to create a transmural window measuring ≥ 1mm long and ≥ .25mm wide in tissue measuring ≥ 2.0mm thick when the device is used in conjunction with the labeled electrosurgical unit at the required electrical settings.
	Torque Strength	The distal tip of the device was fixed, and the proximal end of the device was rotated until failure. The number of rotations to failure and the failure mode were characterized.
	Torque Response	The catheters were rotated 360° clockwise and 360° counterclockwise within the anatomic model, and the process was repeated four times. The torque response was evaluated.
	Visual Inspection	Following simulated use, devices must be free from any damage that would prevent it from normal function/use and devices must meet performance requirements established for all subsequent verification tests.

<table>
<tr><td colspan="2">Tensile Strength</td><td>• Bonds/joints shall maintain mechanical integrity during use
• Each bond/joint was tested against specifications based on the clinical use of the device</td></tr>
<tr><td colspan="2">Corrosion Resistance</td><td>Metallic components of the catheter intended for fluid path contact shall show no signs of corrosion.</td></tr>
<tr><td colspan="2">Leak Testing</td><td>• Air shall not leak into the hub assembly during aspiration
• The hub or catheter shall not leak liquid</td></tr>
<tr><td colspan="2">Catheter Lubricity</td><td>The LTL for average pull force over five cycles will be < 50g when tested over a 10cm distance and 500g pinch force.</td></tr>
<tr><td colspan="2">Visual Inspection</td><td>Catheters must be free from any damage that would prevent it from normal function or use. This includes, but is not limited to fractures, cracks, kinks, tears, loose components, or inadvertent electrode deployment.</td></tr>
<tr><td colspan="2">Radiopacity</td><td>Visibility of the device and alignment under fluoroscopy was demonstrated by representative images taken during the animal studies.</td></tr>
<tr><td rowspan="2">Coating Integrity Testing</td><td>Coating Durability and Coverage</td><td>Coated venous and arterial catheters were stained with (b) (4) dye and evaluated for stain coverage after moderate finger rubbing. All test samples exhibited at least 90% stain coverage.</td></tr>
<tr><td>Particulate Analysis</td><td><table>
<tr><td rowspan="2">Test Group</td><td colspan="3">Average # of Particles (Per device pair)</td></tr>
<tr><td colspan="3">Diameter Size Range (µm)</td></tr>
<tr><td>≥ 10</td><td>≥ 25</td><td>≥ 50</td></tr>
<tr><td>Initial (T = 0)</td><td>6382</td><td>238</td><td>14</td></tr>
<tr><td>Aged (T = 1yr)</td><td>3171</td><td>152</td><td>20</td></tr>
</table></td></tr>
<tr><td rowspan="3">Electrical Plug Testing</td><td>Cord Tensile Strength</td><td>Peak tensile strength between the plug and the cord must be ≥ 5 lbf.</td></tr>
<tr><td>Shroud Tensile Strength</td><td>Peak tensile strength between the plug and the shroud must be ≥ 5 lbf.</td></tr>
<tr><td>Shroud Compressive Strength</td><td>Peak compressive strength between the plug and the shroud must be ≥ 5 lbf.</td></tr>
</table>

PERFORMANCE TESTING – ANIMAL &/OR CADAVER

Two main groups of studies were conducted to support the development of the everlinQ® endoAVF System: (1) early testing using an early version of the device in a cadaver study along with three non-GLP acute animal studies and (2) a concluding eight-animal GLP chronic and acute study using the final device.

The non-GLP acute animal studies and cadaver study used an early version of the device that was similar to the final device design. These studies demonstrated that an endoAVF could be successfully created, there was no unintended tissue damage, and no thrombus formation was observed. These studies also demonstrated that the device could be successfully delivered to the desired location of the AVF using the labeled accessories and that the device was easy to use. The design and results of the GLP study are summarized in Table 4 below. The GLP study demonstrated that the endoAVF could be created safely with adequate blood flow through the fistula and no adverse

histopathological findings at 30 days.

Table 4: Summary of GLP Preclinical Study

Purpose	Methods	Results
Evaluate the acute and chronic safety, fistula blood flow characteristics, fistula patency, handling characteristics, visibility under fluoroscopy, thrombus formation, and histopathological response at the treatment site and off-target tissue sites of the final device design according to Good Laboratory Practices	• GLP • N=8 ovine models (N=4 acute study, N=4 chronic study). Acute Study • Insert, track, deploy, and activate device to create a single AVF in N=2 ovine models, then procedure time and energy delivery were recorded. • After creation, fistulas evaluated (by ultrasound, thermal dilution and/or fluoroscopy via contrast injection) to determine patency and fistula flow. • After 0-1 hour survival, necropsy performed to ensure no downstream tissue effects. • AVF site, vessels and tissue in proximity were histologically examined to characterize these tissues. • Insert, track, deploy, and activate device to create 4 or 5 AVFs in N=2 additional ovine models. • After 0-1 hour survival, necropsy performed in which the vessels were identified and AVFs photographed. Chronic Study • Insert, track, deploy, and activate device to create a single AVF in N=4 ovine models. • After creation, fistulas evaluated (by ultrasound, thermal dilution and/or fluoroscopy via contrast injection) to determine patency and fistula flow. • After 30 days survival, fistulas again examined to determine patency and fistula flow. • Necropsy performed to ensure no downstream tissue effects. • AVF site, vessels and tissue in	• 14/15 attempts to create fistulas in the 8 animals were successful. One attempt failed due to a procedural mistake related to the ovine vasculature, and is not relevant to the intended human anatomy. • All animals survived to the prescribed in-life survival. • There was no morbidity or major unanticipated events that were related to the use of the device. • Fistulas were shown to be patent at 30 days following AVF creation using fluoroscopic imagery. • Blood flow was observed after fistula creation and at 30 days. • There was no evidence of mechanical or thermal injury extending beyond the immediate treatment site following the procedure, and fistula sites appeared to heal well by 30 days. • Arterial and venous ostia appeared acceptably uniform in size and appearance. • No gross findings in off-target or downstream tissues which were indicative of device or treatment related events. • Histopathology in acute animals was negative for thromboembolic events in the lungs or coronary bands. • Post-procedure histopathology of treatment sites showed focal perforations in the artery and vein with perivascular hemorrhage into surrounding fat, as well as treated edges of the ostia characterized by focal mild compressions and subtle thermal coagulation. The observations appeared to be expected for the AVF creation procedure and resolved with time. • Histopathology at 30 days showed the fistulae were patent and maturing, with no evidence of thromboemboli generation, vascular remodeling, or injury. • No bleeding was observed at 30 days. • No histopathological observations related to the device were noted in the heart.

	proximity were histologically examined to characterize these tissues. • Mechanical and thermal injury, inflammation, fibrin/thrombus, fibrosis, mineralization, necrosis, hemorrhage, and intimal proliferation were evaluated. • Gross pathology of treatment sites, subcutaneous tissues on the downstream distal limb, and systemic organs in acute and chronic studies. • Histopathology of acute treatment sites, chronic treatment sites, lungs, and heart.	• No histopathological findings related to device safety were observed in the lungs. One small, localized fat embolus was observed but was asymptomatic and deemed to be coincidental as it has not been observed to occur during percutaneous interventional procedures in the arteries or veins in humans.

SUMMARY OF CLINICAL INFORMATION

The everlinQ® System was primarily supported by a pivotal study entitled the "Novel Endovascular Access Trial" (NEAT Study). In addition, a supportive global analysis of clinical use of the everlinQ® System ("Global Analysis") was conducted that included data from 4 prospective clinical studies (FLEX, NEAT, EU PMCF and EASE) and 1 commercial use data set (COMM). A pooled analysis of the 4 prospective clinical studies was also presented. Details of the study designs and key clinical outcomes are provided in the following sections. The study names are defined as follows:

- FLEX – A Prospective Pilot Clinical Evaluation of the TVA FLEX-1 Device
- NEAT – Novel Endovascular Access Trial
- EU PMCF – Post Market Study of the everlinQ® endoAVF System
- EASE – everlinQ® Endovascular Access System Enhancements Study
- COMM – commercial use data set

Table 5: Clinical Data Sources

Data Source	Device Studied	Dates of Index Procedures	# Sites (Countries)	Total Subjects	Subjects in Pooled Analysis[5]	
					Safety	Effectiveness
FLEX[1]	6Fr FLEX-1	Aug 2012-Sep 2013	1 (Paraguay)	33	33	33
NEAT	6Fr everlinQ®	Jan 2014- Aug 2015	6 (Canada) 2 (Australia)	60	60	60
EASE[2]	4Fr everlinQ®	May 2016 - Nov 2016	1 (Paraguay)	32	0	32
EU-PMCF	6Fr everlinQ®	Sep 2016 - Aug 2017	5 (Germany) 3 (England)	32	32	32
COMM- All[3]	6Fr everlinQ®	Feb 2015 - Jun 2017	4 (England) 16 (Germany)	79	0	0

COMM – Cannulated[4]		Feb 2015 - Aug 2017	1 (Netherlands) 1 (Switzerland)	45	0	0
Total Subjects[5]				**236**	125	157

1. The FLEX-1 device was a previous version of the subject device. After the FLEX Study, design modifications were made to improve ease of use (i.e. handle ergonomics and user interface). The overall mechanism of action and device function for creating an endoAVF has remained the same throughout all revisions of the 6Fr FLEX-1 and everlinQ® devices.

2. The EASE subjects were not included in the Pooled Safety Population, since the 4Fr system is a different product compared to the 6Fr systems used in the other data sources.

3. No COMM subjects were included in the Pooled Safety or Effectiveness Populations because baseline data were unavailable in the commercial cases, precluding pooling.

4. The COMM-Cannulated cases comprise the subset of COMM-All cohort where follow-up data were collected, including safety data and cannulation data.

5. The total number of subjects is less than the sum of the "Total Subjects" column because the COMM – Cannulated subject cohort is a subset of all the commercial subjects included in the COMM-All data.

Primary Clinical Data Set: NEAT Study

Objective: The purpose of the NEAT Study was to evaluate the safety and effectiveness of the everlinQ endoAVF System among subjects undergoing endoAVF creation.

Study Design: The NEAT study was a prospective, single-arm, multi-center study that enrolled 60 "study cohort" subjects and 20 "roll-in" subjects at 9 sites in Canada, Australia and New Zealand. Candidates for this study were subjects with chronic kidney disease (CKD) who required a hemodialysis vascular access.

Eligibility Criteria Summary: The study population consisted of male and female patients from Canada, Australia, and New Zealand who had chronic kidney disease (CKD), required a hemodialysis vascular access, and were at least 18 years of age.

Key inclusion criteria included the following:

- Established, non-reversible kidney failure requiring hemodialysis.
- Patients deemed eligible for a native arteriovenous fistula.
- Target artery diameter and target vein diameter both ≥ 2.0 mm.
- Estimated life expectancy > 1 year.
- Subject was free of clinically significant conditions or illness within 30 days prior to the AV fistula that may compromise the procedure.

Key exclusion criteria included the following:

- Subjects who are eligible for a distal forearm fistula were excluded from the study. Exception: If a distal forearm fistula had failed or distal forearm fistula was not the most optimum choice the subject was considered eligible to enroll.
- Known central venous stenosis or central vein narrowing > 50% based on imaging on the same side as the planned AVF creation.
- Upper extremity venous occlusion(s) and/or vessel abnormality(ies) on the same side as the planned AVF creation that precludes endovascular AVF creation by everlinQ endoAV System as deemed by the interventionalists' clinical judgment.
- At the time of procedure distance between target artery and vein will not allow magnets to align vessels sufficiently to create the fistula.
- Prior upper arm surgically created access or functioning surgical access in the planned treatment arm.
- Subjects with Body Mass Index (BMI) >35 who, in an expert cannulator's opinion, are not appropriate candidates for cannulation.
- "Planned" concomitant major surgical procedure within 6 months of enrollment or previous major surgery within 30 days of enrollment.
- Immunosuppression, defined as use of immunosuppressive medications used to treat an active condition.
- New York Heart Association (NYHA) class III or IV heart failure.

Demographics: The total Intent-to-Treat (ITT) population consisted of 60 subjects. Data about the patient demographics and baseline comorbidities are provided in the tables below.

Table 6: NEAT Study Subject Demographics

Characteristic	Summary
Gender	
Male	65.0% (39/60)
Female	35.0% (21/60)
Age (years)	59.9 ± 13.6 (60) 61.0 [28.0, 85.0]
BMI	27.9 ± 6.1 (60) 27.1 [16.1 ,44.1]
BMI > 25	63.3% (38/60)
Target Dialysis Weight (kg)	80.9 ± 21.9 (60) 78.7 [43.0, 138.9]
Race	
Caucasian	60.0% (36/60)
Asian	31.7% (19/60)
Native Hawaiian/Pacific Islander	1.7% (1/60)
Other	6.7% (4/60)
Smoker (current or previous)	33.3% (20/60)
Previous AVF (prior to study)	31.7% (19/60)
Same arm as used for endoAVF creation	73.7% (14/19)
Contralateral arm as used for endoAVF creation	26.3% (5/19)
Pre-dialysis	56.7% (34/60)
Data displayed as Mean±SD (N);Median [Range] or % (n/N).	

Table 7: NEAT Study Baseline Comorbidities

Medical Condition/Comorbidity	Summary % (n/N)
Primary Diagnosis Causing ESRD:	
Diabetes	50.0% (30/60)
Glomerular based disease	13.3% (8/60)
Hypertension	15.0% (9/60)
Interstitial nephritis	1.7% (1/60)
Polycystic kidney disease	6.7% (4/60)
Other	11.7% (7/60)
Unknown	1.7% (1/60)
Comorbidities:	
Chronic Obstructive Pulmonary Disease (COPD)	3.3% (2/60)
Cerebrovascular Disease (CVA/TIA)	15.0% (9/60)
Congestive heart failure (NYHA I or II)	11.7% (7/60)
Coronary artery disease (CAD)	21.7% (13/60)
Diabetes	65.0% (39/60)
Hypertension	91.7% (55/60)
Hyperlipidemia	48.3% (29/60)
Malignancy	18.3% (11/60)
Prior peritoneal dialysis	30.0% (18/60)
Prior renal transplant	13.3% (8/60)

Accountability: A total of 183 subjects were screened for participation in the study. Sixteen (16) patients declined to participate and 84 patients failed initial screening. Three (3) additional patients failed final enrollment criteria (distance between target artery and vein too great at time of procedure) and were excluded at the time of index procedure. Most subjects who were excluded from the study did not meet the target vessel criteria of ≥ 2mm. In total, 80 subjects were enrolled in the study; 60 subjects were included in the study cohort and 20 subjects comprised a roll-in cohort.

Figure 3 below depicts the subject disposition in the NEAT Study. The figure shows the number of subjects who were evaluated or exited the study at each time point. Among the 60 study cohort subjects, 3 subjects (5%) died during the study and 8 (13.3%) withdrew for other reasons. A total of 11 subjects (18.3%) exited the study before the 12-month follow-up time point, and 4 additional subjects (6.7%) were not yet eligible for their 12-month evaluation at the time the final NEAT study report was submitted.

In total, 45/60 subjects (75%) were evaluated at 12 months. Those 45 subjects included 24 pre-dialysis subjects (24/34 = 70.6% of pre-dialysis subjects) and 21 dialysis subjects (21/26 = 80.8% of dialysis subjects).

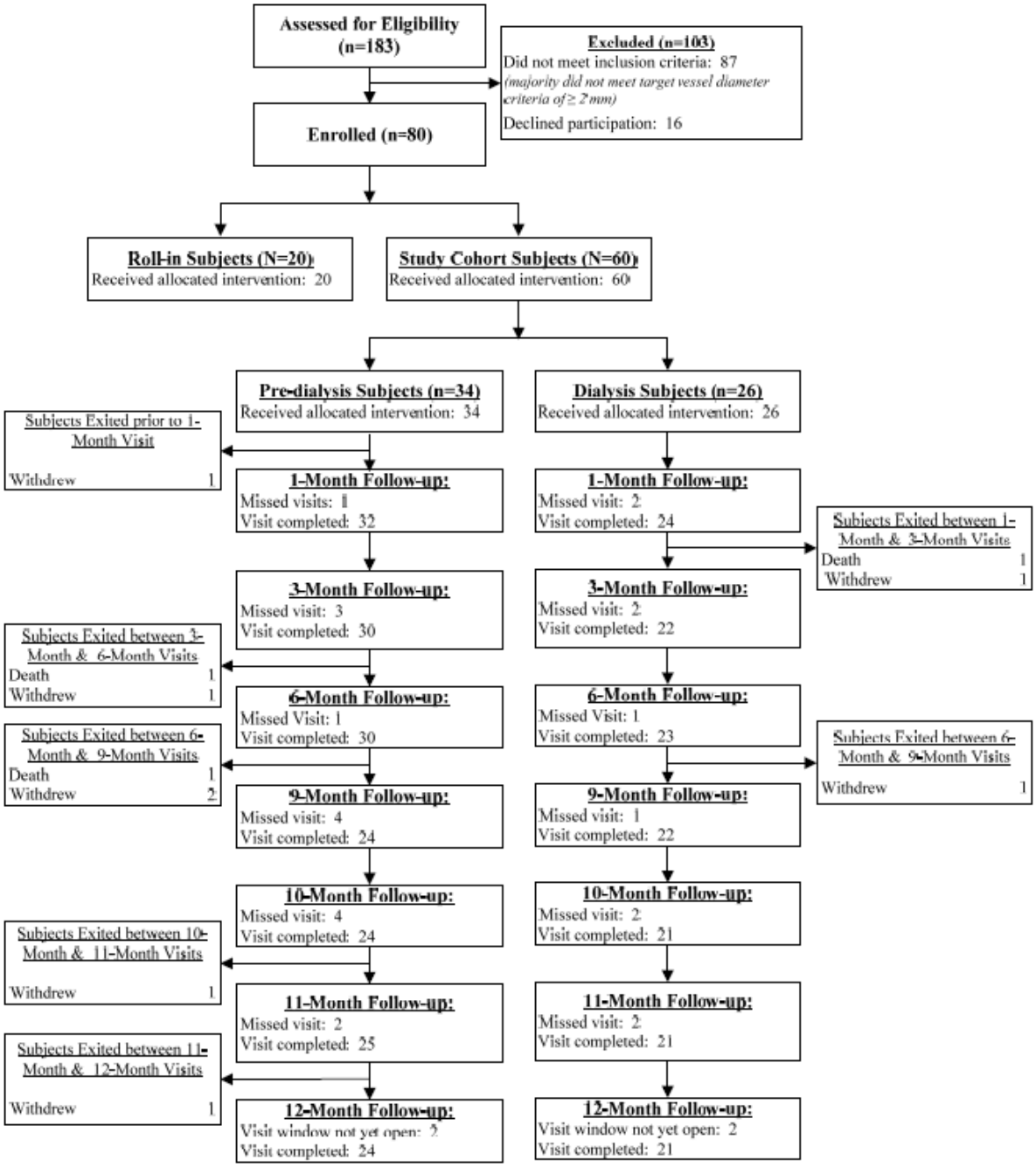


Figure 3: NEAT Study Subject Disposition Through End of Study

Primary Endpoints

1) Safety: The safety endpoint was the percentage of patients who experienced one or more serious study device related adverse events during the first 3 months following AVF creation as adjudicated by an independent Clinical Events Committee (CEC). There was no formal hypothesis test associated with the safety endpoint. Analysis of the safety endpoint was performed on the study cohort subjects.

The following definitions were used for the safety analyses:

- Adverse event (AE): any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.

- Serious adverse event (SAE): A serious adverse event was defined as an adverse event that:
  a) Led to death,
  b) Led to serious deterioration in the health of the subject, that either resulted in
     i. a life-threatening illness or injury, or
     ii. a permanent impairment of a body structure or a body function, or
     iii. in-patient or prolonged hospitalization, or
     iv. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
  c) led to foetal distress, foetal death or a congenital abnormality or birth defect

  NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the Study Protocol, without serious deterioration in health, was not considered an SAE.

2) Effectiveness: The primary endpoint of the study was the percentage of patients with fistula maturation/usability at 3 months post-procedure, defined as endoAVF that is free of stenosis or thrombosis, with brachial artery flow of at least 500 ml/min and at least 4 mm vein diameter (as measured by duplex ultrasound) OR patient was dialyzed using 2 needles.

Note: stenosis and thrombosis were defined as flow limiting complications that led to fistula closure at any time during the first 3 months post index procedure. Dialysis using 2 needles were assessed at any time during the first 3 months post index procedure.

This composite endpoint was chosen based on the most common three reasons for AVF failure to mature or lack of AVF usability: 1) thrombosis, 2) stenosis and 3) inadequate flow or diameter of the vein leading to abandoned AVF.

The primary effectiveness endpoint was tested for all 60 study cohort subjects ("Enrolled" population). Subjects in whom an endoAVF was attempted (i.e. RF energy was applied) but not created were included in the analysis as failures. If a patient had missing endpoint data, due to reasons not related to the endoAVF, procedure, or device, they were not included in the primary analysis.

The formal hypothesis tested for the primary endpoint was the 3-months proportion of patients with fistula maturation/usability greater than a historically derived performance goal:

$$H_0: \pi \leq 57.5\% \text{ vs. } H_A: \pi > 57.5\%,$$

where π is the proportion of patients with fistula maturation/usability and 57.5% is the historically derived performance goal (PG). The PG was derived based on surgical AVF failure rates reported in clinical literature.

The number and percentage of patients with fistula maturation/usability within 3 months were summarized. A 90% exact confidence interval (CI) was calculated. The lower bound of the confidence interval was compared to the performance goal of 57.5% to determine success.

Secondary Endpoints

Secondary endpoints were summarized using descriptive statistics. There were no formal hypotheses associated with these endpoints and these analyses were not statistically powered. Analyses for each endpoint were performed on the study cohort subjects unless otherwise noted.

- *Procedural success:* The successful endoAVF creation rate as assessed via fistulogram immediately post-procedure or duplex ultrasound, or via presence of thrill/bruit.

- *Time to Fistula Maturation:* the number of days between the date of AVF creation and the date of endoAVF maturation (based on primary efficacy endpoint definition of maturation).

- *Duration of Central Venous Catheter (CVC) Exposure:* The rate of CVC use at 1, 2, 3, 6 and 12 months follow-up. The analysis was performed for pre-dialysis and on dialysis subjects.

- *endoAVF-related Interventions Rate:* The intervention rate for endoAVF (defined as any intervention required to maintain or re-establish patency; may be also referred as "re-intervention" rate) was calculated at 3, 6 and 12 months post index procedure.

- *Primary Patency:* The primary patency rate was determined via Kaplan-Meier methods and based on the time of endoAVF creation until any intervention designed to maintain or re-establish patency or endoAVF abandonment.

- *Secondary Patency:* The secondary patency rate was determined via Kaplan-Meier methods and based on the time of endoAVF creation until access abandonment.

- Additional analyses were summarized using descriptive statistics:
    - Rate of serious procedure-related AEs at 3 and 6 months.
    - Rate of serious device-related AEs at 6 months.
    - Rate of device and/or procedure-related infections at 6 months.
    - Arterial flow rates and diameters as measured via DUS at 3, 6 and 12 months post index procedure.
    - Subject satisfaction and quality of life parameters via Vascular Access questionnaire.
    - The percentage of subjects dialyzed using endoAVF (2 needles) for 2/3 of their dialysis sessions over a 4-week period.

Results: The principal safety and effectiveness results from patients in the study are provided below. The analyses were performed on all 60 study cohort subjects (excluding roll-in subjects) unless otherwise noted.

Primary Safety Endpoint: At 3 months post index procedure, only one subject experienced one serious device related event (pseudoaneurysm), resulting in an observed percentage of 1.67% (1/60) with a two-sided 95% exact binomial confidence interval of 0.04% - 8.94%.

Primary Effectiveness Endpoint: The primary effectiveness endpoint results are shown in the table below. The primary endpoint was met with a 90-day maturation success rate of 52/57 (91.2%).

Table 8: Primary Effectiveness Endpoint Results – 90-Day Maturation Success Rate

	Subject Success % (n/N)	Exact 90% Confidence Interval	Hypothesis	Decision	Conclusion
Subject with endoAVF that is free of stenosis or thrombosis[i], with brachial artery flow of at least 500 ml/min and at least 4 mm vein diameter OR subject was dialyzed using 2 needles	91.2% (52/57)	(82.4%, 96.5%)	H_O: $p_S \leq 57.5\%$ H_A: $p_S > 57.5\%$	Reject H_O	Performance Goal Met
[i]As adjudicated by the CEC.					

The primary effectiveness analysis did not include 3 subjects who either died prior to the 90-day evaluation, unrelated to the device or procedure (1 subject) or experienced a procedural complication that led to endoAVF sacrifice (2 subjects).

If all 60 study cohort subjects were included in the primary endpoint analysis, the primary endpoint result was 52/60 = 86.7%. The primary endpoint was still met (90% CI: 77.2-93.2%).

Secondary Endpoints: A summary of the secondary endpoint analyses are provided below. All analyses presented below are based on the ITT population unless otherwise noted.

- *Procedural Success:* Procedural success was achieved in 59/60 subjects (98.3%) per the definition above.

- *Time to Fistula Maturation:* The mean time to maturation based on the endpoint criteria was 14.8 days. Additional details are provided in the table below.

Table 9: Time to Fistula Maturation

Maturation Time	Mean ± SD (N) Median [Range]
Days to endoAVF maturation based on DUS	14.8 ± 26.0 (52) 5.0 [1.0, 97.0]
Days to endoAVF maturation based on physical exam	65.0 ± 44.3 (45) 58.0 [26.0, 213.0]

- *Duration of Central Venous Catheter (CVC) Exposure:* CVC exposure was evaluated for both pre-dialysis subjects and subjects who were on dialysis. Table 10 below shows the number of subjects who had a CVC in place at each timepoint. In sum, the total NEAT study CVC exposure at 12 months was 14/60 subjects (23.3%), calculated by adding 4/35 CVC only + 0/35 CVC and endoAVF subjects from the pre-dialysis subset, in addition to 6/25 CVC-only + 4/25 CVC and endoAVF subjects from the post-dialysis subset.

Table 10: Duration of CVC Exposure

Pre-Dialysis Subjects	
1-Month (0-45 Days)	
CVC only	3/35 (8.6%)
endoAVF only	0/35 (0.0%)
CVC + endoAVF	0/35 (0.0%)
Other	0/35 (0.0%)
3-Month (46-135 Days)	
CVC only	3/35 (8.6%)
endoAVF only	8/35 (22.9%)
CVC + endoAVF	2/35 (5.7%0
Other	0/35 (0.0%)
6-Month (136-270 Days)	
CVC only	3/35 (8.6%0
endoAVF only	8/35 (22.9%)
CVC + endoAVF	4/35 (11.4%)
Other	1/35 (2.9%)
12-Month (271-390 Days)	
CVC only	4/35 (11.4%)
endoAVF only	10/35 (28.6%)
CVC + endoAVF	0/35 (0.0%)
Other	1/35 (2.9%)
Post-Dialysis Subjects	
1-Month (0-45 Days)	
CVC only	24/25 (96.0%)
endoAVF only	0/25 (0.0%)
CVC + endoAVF	0/25 (0.0%)
Other	1/25 (4.0%)
3-Month (46-135 Days)	
CVC only	9/25 (36.0%)
endoAVF only	1/25 (4.0%)
CVC + endoAVF	13/25 (52.0%)
Other	1/25 (4.0%0
6-Month (136-270 Days)	
CVC only	4/25 (16.0%)
endoAVF only	6/25 (24.0%)
CVC + endoAVF	12/25 (48.0%)

Other	4/25 (16.0%)
12-Month (271-390 Days)	
CVC only	6/25 (24.0%)
endoAVF only	11/25 (44.0%)
CVC + endoAVF	4/25 (16.0%)
Other	4/25 (16.0%)

- *endoAVF-related Interventions Rate*: Table 11 below shows the number and types of adjunctive procedures that were performed at the same time as the endoAVF index procedure. In total, 56/60 subjects (93.3%) required the implantation of at least one coil in their brachial vein at the time of the index procedure to redirect blood flow to the superficial veins and support maturation of the target cannulation area. The mean number of coils used per subject who received them was 1.6, with a range of 1.0-3.0 coils.

  Table 12 shows the number of subjects who required at least one reintervention after the index procedure to assist maturation of the endoAVF or to maintain a mature endoAVF. The total number and types of reinterventions are also tabulated.

Table 11: Adjunctive Procedures Performed at Index Procedure

Adjunctive Procedure	# of Subjects (%)
Therapeutic embolization	56 (93.3%)
Arterial closure device use	41 (68.3%)
PTA	0 (0.0%)
Stent	0 (0.0%)
Other*	6 (10.0%)
Total Subjects with ≥ 1 Procedure	58/60 (96.7%)
* Other procedures include thrombolysis (1), thrombectomy (2), new surgical AVF (1), open surgical repair for an intraoperative complication (6). Adjunctive procedures are tabulated by the procedure (i.e. one subject may have more than one adjunctive procedure), except for the last row which tabulates the data at the subject level.	

Table 12: endoAVF-related Reinterventions in NEAT Study

Reintervention	Indication	0-90 Days	0-180 Days	0-365 Days
Coil Embolization	Maturation Assistance	2	2	5
Angioplasty	Maturation Assistance	1	1	2
Transposition	Facilitate Cannulation	0	3	5
Surgical Fistula or Graft	New Access Needed	0	0	2
EndoAVF Ligation	Adverse Event	3	3	3
Thrombin Injection for Pseudoaneurysm	Adverse Event	2	2	2
Surgical Procedure for Complication	Adverse Event	1	1	1
Total Reinterventions	-	9	12	20
Total Subjects with ≥ 1 Reintervention	-	7/60 (11.7%)	10/60 (16.7%)	17/60 (28.3%)

- *Primary Patency*: The following primary patency rates were reported:
  - Primary patency, 6 months: 81.1%

- Primary patency, 12 months: 73.4%
- Assisted primary patency, 6 months: 84.8%
- Assisted primary patency, 12 months: 77.2%

- *Secondary Patency:* The following secondary patency rates were reported:
  - Secondary patency, 6 months: 86.4%
  - Secondary patency, 12 months: 78.9%

Additional Analyses

Rate of Serious Device- and Procedure-Related AEs

A total of eight (8) serious adverse events (SAEs) in five (5) subjects were adjudicated as procedure and/or device-related. All eight (8) SAEs were adjudicated as procedure-related, and one of the eight (1/8) SAEs (pseudoaneurysm near endoAVF) was adjudicated as related to both the device and the procedure. Seven of the eight (7/8) SAEs occurred within 24 hours of the index procedure. One (1) SAE (steal syndrome) occurred on Day 8 post index procedure, representing the maximum number of days post-index procedure for onset of a serious procedure-related event. A summary of SAEs related to the study procedure and/or device has been provided in Table 13 below.

All SAEs were able to be resolved through intervention or resolved on their own. There were no instances of permanent impairment associated with the device. No new serious procedure and/or device related events were reported beyond 3 months.

Table 13: NEAT Study SAEs Related to Study Procedure and/or Device (CEC-Adjudicated)

	0-3 Months		3-6 Months		> 6 Months		Overall	
Events[i]	Total Events	Subjects Experienced % (n/N)	Total Events	Subjects Experienced % (n/N[ii])	Total Events	Subjects Experienced % (n/N[iii])	Total Events	Subjects Experienced % (n/N)
Overall	8	8.3% (5/60)	0	0.0% (0/57)	0	0.0% (0/55)	8	8.3% (5/60)
Closure device embolization	2	3.3% (2/60)	0	0.0% (0/57)	0	0.0% (0/55)	2	3.3% (2/60)
Dissection of brachial artery	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Pseudoaneurysm near endoAVF[iv]	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Pseudoaneurysm, access site	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Steal syndrome	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Thrombosis brachial artery, not leading to fistula closure	2	3.3% (2/60)	0	0.0% (0/57)	0	0.0% (0/55)	2	3.3% (2/60)

[i] As adjudicated by an independent CEC.
[ii] Based on the number of subjects still in the study at 3 Month follow-up (i.e. subjects who exited the study after 3 Month follow-up window opened).
[iii] Based on the number of subjects still in the study at 6 Month Follow-up (i.e. subjects who exited the study after 6 Month follow-up window opened).
[iv] This event is also related to the study device.

A total of 28 adverse events (AEs) in 22 subjects were adjudicated as non-serious and procedure and/or device-related. Of these AEs, all were adjudicated as procedure-related (28/28) and three were adjudicated as related to both the device and the procedure (3/28). Twenty-six of the related AEs (26/28) occurred within 3 months of the index procedure. A summary of the non-serious AEs is provided in Table 14 below.

All but two procedure-related AE occurred within 3 months post-index procedure resulting in 3-month procedure-related AE rate of 33.3% (20/60) and overall rate of 36.7% (22/60) through 12 months.

Table 14: NEAT Study Non-Serious Procedure-Related Adverse Events by Type and Timing (CEC-Adjudicated)

	0-3 Months		3-6 Months		> 6 Months		Overall	
Events[i]	Total Events	Subjects Experienced % (n/N)	Total Events	Subjects Experienced % (n/N[ii])	Total Events	Subjects Experienced % (n/N[iii])	Total Events	Subjects Experienced % (n/N)
Overall	26	33.3% (20/60)	2	3.5% (2/57)	0	0.0% (0/55)	28	36.7% (22/60)
Bruising	6	10.0% (6/60)	0	0.0% (0/57)	0	0.0% (0/55)	6	10.0% (6/60)
Hematoma	4	6.7% (4/60)	0	0.0% (0/57)	0	0.0% (0/55)	4	6.7% (4/60)
Numbness, tingling and/or coolness in the fistula extremity	3	5.0% (3/60)	0	0.0% (0/57)	0	0.0% (0/55)	3	5.0% (3/60)
Pain	2	3.3% (2/60)	0	0.0% (0/57)	0	0.0% (0/55)	2	3.3% (2/60)
Perforation, related to guidewire	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Pseudoaneurysm near endoAVF	2	3.3% (2/60)	0	0.0% (0/57)	0	0.0% (0/55)	2	3.3% (2/60)
Pseudoaneurysm, access site	2	3.3% (2/60)	0	0.0% (0/57)	0	0.0% (0/55)	2	3.3% (2/60)
Spasm and clot	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Steal	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Swelling, irritation or pain	2	3.3% (2/60)	1	1.8% (1/57)	0	0.0% (0/55)	3	5.0% (3/60)
Thrombosis Brachial artery, Not leading to fistula closure	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)
Thrombosis post proc of endoAVF leading to fistula closure	0	0.0% (0/60)	1	1.8% (1/57)	0	0.0% (0/55)	1	1.7% (1/60)
Thrombosis, intra-procedural leading to fistula closure	1	1.7% (1/60)	0	0.0% (0/57)	0	0.0% (0/55)	1	1.7% (1/60)

[i] As adjudicated by the Clinical Events Committee.
[ii] Based on the number of subjects still in the study at 3 Month follow-up (i.e. subjects who exited the study after 3 Month follow-up window opened).
[iii] Based on the number of subjects still in the study at 6 Month Follow-up (i.e. subjects who exited the study after 6 Month follow-up window opened).

Summary of Occlusions and Thromboses

Table 15 below provides a summary of the number of thromboses and occlusions that occurred during the study. The data are presented as acute (defined as 0-42 days to represent the data reported through the 6-week visit) and total events reported through the end of the study's 12-month visit. There was 1 acute thrombosis of the endoAVF treated unsuccessfully with thrombolysis, and the endoAVF was eventually abandoned. There were 4 additional (non-acute) thromboses of the endoAVF all leading to endoAVF abandonment. In total, 5/60 (8.3%) subjects experienced thrombosis of the endoAVF at some point during the study. 3/60 (5.0%) subjects experienced thrombosis of the brachial artery during the study. All 3 of these events were acute and were treated (1 thrombolysis, 2 thrombectomy) and did not lead to endoAVF abandonment. 1/60 (1.7%) subjects experienced occlusion of the endoAVF during the study. This event was non-acute and led to endoAVF abandonment. There were no occlusions of the brachial artery during the study.

All 4 acute thrombosis events listed in Table 15 (1 endoAVF thrombosis and 3 brachial artery thromboses) occurred at the time of the endoAVF index procedure and all were treated via thrombolysis or thrombectomy.

The events were either treated with thrombectomy/thrombolysis or no treatment was provided. 6/9 of the endoAVFs that experienced an occlusion or thrombosis were abandoned, for a total endoAVF abandonment rate of 10.0% at 12 months.

Table 15: NEAT Study Thromboses and Occlusions

	Acute		Total		Treatment(s)	Outcome(s)
	N	Abandoned	N	Abandoned		
Thrombosis – endoAVF	1/60 (1.7%)	1/1	5/60 (8.3%)	5/5	1 Thrombolysis 4 No Treatment	2/5 subjects entered study pre-dialysis and exited study pre-dialysis 3/5 subjects entered study on-dialysis and exited study on CVC
Thrombosis – Brachial Artery*	3/60 (5.0%)	0/3	3/60 (5.0%)	0/3	2 Thrombectomy 1 Thrombolysis	2/3 subjects entered study pre-dialysis and 1 subject exited study on CVC and 1 subject exited study early pre-dialysis 1/3 subjects entered study on-dialysis and exited study on endoAVF and achieved functional cannulation success
Occlusion – endoAVF	0/60 (0.0%)	-	1/60 (1.7%)	1/1	1 No Treatment	1/1 subject entered study pre-dialysis and exited study early pre-dialysis
Occlusion – Brachial Artery	0/60 (0.0%)	-	0/60 (0.0%)	-	-	-
Total – endoAVF	1/60 (1.7%)	1/1	6/60 (10.0%)	6/6	-	-
Total - All	4/60 (6.7%)	1/4	9/60 (15.0%)	6/9	-	-
* - The brachial artery thrombosis events occurred during the index procedure.						

Rate of Device and/or Procedure-Related Infections

There were no device- or-procedure related infections observed in the study. There were two subjects (2/60 = 3.3%) who experienced an infection related to a CVC.

Arterial Flow Rates and Vein Diameters

Table 16 below shows the arterial flow rates through the brachial artery as measured by DUS, expressed as mL/min. The highest mean arterial flow rate was observed at 6 weeks (928.17 mL/min). Figure 4 shows the average brachial artery flow rates over time. Table 17 shows the inner diameters by vessel and study visit, expressed in millimeters (mm).

Table 16: Brachial Artery (Medial) Flow Rates by Study Visit

Study visit	Flow Rate (peak)	Flow Rate (mean)
Baseline	123.40 ± 100.45 (57) 102.10 [8.20,620.00]	81.48 ± 61.67 (56) 58.60 [8.29,300.00]
1-7 Days	1188.04 ± 768.76 (57) 1105.00 [14.35,4029.50] P-value: <.0001	785.38 ± 474.35 (59) 743.50 [7.46,2259.50] P-value: <.0001
1 Month	1358.03 ± 753.33 (55) 1290.00 [25.00,3026.00] P-value: <.0001	881.25 ± 507.74 (54) 838.00 [25.00,2713.50] P-value: <.0001
6 Weeks	1391.72 ± 1017.27 (9) 923.00 [563.00,3770.00] P-value: 0.0060	928.17 ± 519.75 (9) 822.50 [330.50,2081.00] P-value: 0.0017
3 Months	1521.06 ± 875.51 (48) 1328.50 [22.00,4408.50] P-value: <.0001	917.57 ± 657.02 (48) 827.50 [23.00,4148.00] P-value: <.0001
6 Months	1540.45 ± 1075.16 (47) 1229.50 [260.00,5571.00] P-value: <.0001	893.19 ± 634.68 (47) 754.50 [132.00,3695.00] P-value: <.0001
12 Months	1480.35 ± 883.58 (31) 1289.00 [178.00,3369.00] P-value: <.0001	851.39 ± 521.69 (32) 837.50 [80.65,2807.50] P-value: <.0001
Data summarized as Mean±SD (N); Median [Range]; P-value for change from baseline		

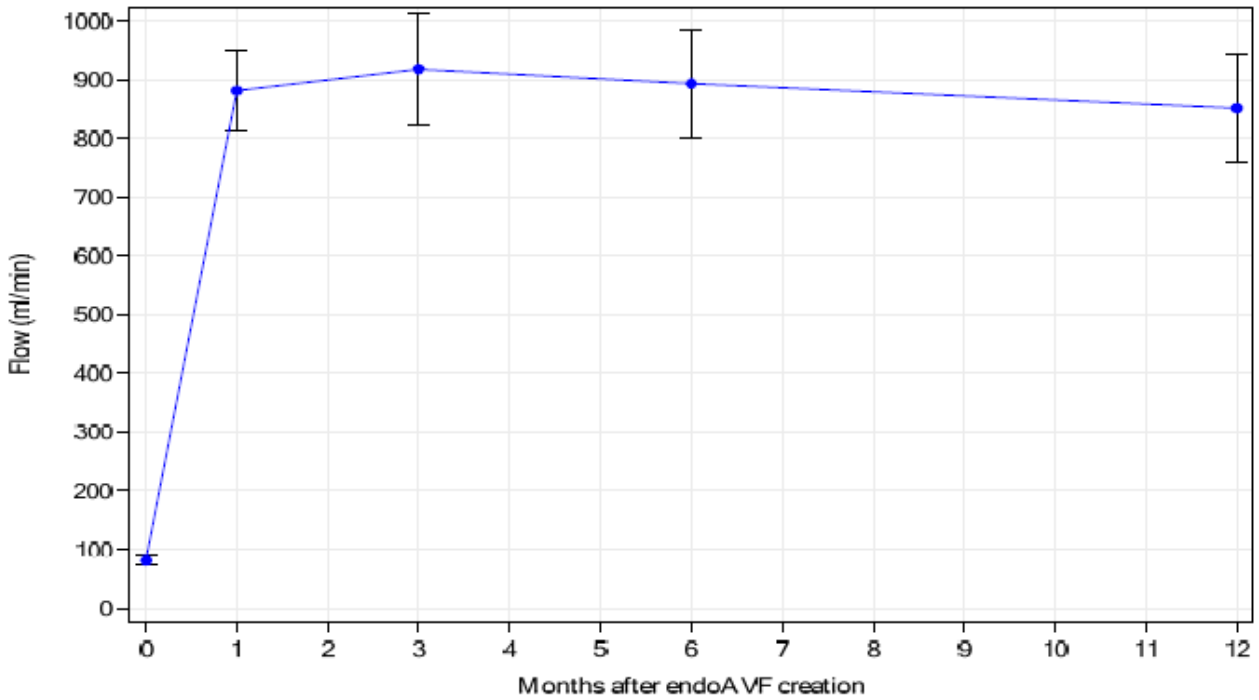


Figure 4: Average Brachial Artery Flow Rate by Month

Table 17: Vessel Inner Diameters by Study Visit

Vessel	Baseline	1-7 Days	1 Month	6 Weeks	3 Months	6 Months	12 Months
Median cubital vein at elbow	4.19 ± 1.48 (60) 3.90 [1.20,8.50]	5.20 ± 1.54 (57) 5.00 [2.90,9.30] P-value: <.0001	5.25 ± 1.89 (54) 4.85 [1.60,10.60] P-value: 0.0001	5.11 ± 1.61 (9) 5.80 [2.40,7.00] P-value: 0.2827	5.89 ± 1.94 (48) 5.90 [2.20,12.60] P-value: <.0001	6.09 ± 1.89 (47) 6.00 [2.80,12.90] P-value: <.0001	6.93 ± 2.47 (32) 6.10 [4.00,15.20] P-value: <.0001
Cephalic vein at 2" proximal of elbow	3.34 ± 1.18 (53) 3.20 [1.20,6.10]	4.31 ± 1.15 (52) 4.40 [1.30,6.50] P-value: <.0001	4.80 ± 1.43 (47) 5.10 [1.60,8.30] P-value: <.0001	5.47 ± 1.38 (7) 5.20 [4.00,8.10] P-value: 0.0652	4.92 ± 1.51 (40) 5.10 [1.70,7.80] P-value: <.0001	5.26 ± 1.59 (41) 5.30 [2.10,8.60] P-value: <.0001	5.57 ± 1.98 (27) 5.40 [1.40,9.30] P-value: <.0001
Cephalic vein at 2" distal of elbow	3.53 ± 1.35 (57) 3.40 [1.20,6.70]	4.44 ± 1.34 (56) 4.60 [1.40,6.70] P-value: <.0001	4.98 ± 1.69 (50) 5.20 [1.30,9.20] P-value: <.0001	5.47 ± 1.83 (9) 5.30 [1.60,7.70] P-value: 0.0044	5.13 ± 1.57 (44) 5.25 [1.60,9.30] P-value: <.0001	5.74 ± 1.62 (43) 5.70 [2.90,9.60] P-value: <.0001	6.15 ± 2.54 (31) 6.10 [1.60,11.60] P-value: <.0001
Cephalic vein (mid)	3.15 ± 1.10 (56) 3.00 [1.10,5.60]	4.30 ± 1.18 (54) 4.40 [1.30,7.00] P-value: <.0001	4.90 ± 1.47 (49) 5.20 [2.40,8.80] P-value: <.0001	5.51 ± 1.14 (8) 5.30 [3.80,7.00] P-value: 0.0005	5.15 ± 1.63 (42) 5.50 [2.00,9.10] P-value: <.0001	5.41 ± 1.57 (44) 5.45 [2.50,8.60] P-value: <.0001	6.12 ± 2.58 (30) 5.70 [1.90,10.60] P-value: <.0001
Basilic vein (medial)	4.17 ± 1.40 (60) 4.00 [1.60,8.00]	5.37 ± 1.32 (59) 5.40 [2.20,8.90] P-value: <.0001	5.86 ± 1.48 (54) 5.80 [2.20,9.00] P-value: <.0001	6.31 ± 1.57 (9) 6.00 [3.90,8.30] P-value: 0.0036	5.99 ± 1.57 (47) 5.90 [3.10,10.50] P-value: <.0001	5.84 ± 1.50 (47) 6.00 [3.10,9.60] P-value: <.0001	6.29 ± 1.41 (32) 6.55 [3.60,8.80] P-value: <.0001
Data summarized as Mean±SD (N); Median [Range]; P-value for change from baseline							

Dialysis Using 2-Needle Cannulation

The following analyses are based on 52 subjects with a usable endoAVF (30 pre-dialysis subjects and 22 on dialysis subjects) at the end of the NEAT Study. A "usable" endoAVF was defined as an endoAVF that met the primary effectiveness endpoint success criteria. In total, 31/60 (52%) of the NEAT Study subjects initiated 2-needle dialysis with the endoAVF during the study.

Two-Needle Dialysis Analysis of Pre-Dialysis Subjects:

There were 30 subjects who entered the study as pre-dialysis subjects and had a usable endoAVF at the end of the study (per primary endpoint definition):

- 16/30 (53.3%) subjects needed dialysis during the course of the study:
  - 14/16 successfully utilized 2-needle dialysis:
    - 12/14 subjects met the criteria for functional fistula cannulation success defined as "cannulating their endoAVF at 2/3 of their dialysis sessions over a continuous 4 week period with 2-needle cannulation."
    - 1 subject's endoAVF was successfully created and determined to be mature. However, due to the subject's fear of needles, self-cannulation was continued via CVC.
    - 1 subject had 2 successful cannulations of endoAVF but expired shortly thereafter due to causes unrelated to the study; and therefore, did not have an opportunity to complete a 4-week functional cannulation study requirement.
  - 1/16 had their endoAVF abandoned prior to the need for dialysis due to steal syndrome leading to fistula ligation.

- 1/16 subject was not able to initiate dialysis with endoAVF despite having a mature fistula 28 days post index procedure since the veins were too deep. Instead of undergoing vein superficialization a permanent CVC was placed. The subject was exited from the study without completing 12 months follow-up. Note this subject was utilizing peritoneal dialysis prior to entering into the study and was exited from the study since the subject went back to peritoneal dialysis.

- 14/30 (46.7%) subjects exited the study without the need for dialysis and therefore, endoAVF cannulation.

Two-Needle Dialysis Analysis of <u>On-Dialysis</u> Subjects:

There were 22 subjects who entered the study on dialysis and had a usable endoAVF at the end of the study (per primary endpoint definition):

- 21/22 on dialysis subjects needed dialysis during the course of the study:
  - 17/21 subjects successfully initiated 2-needle cannulation:
    - 8 subjects started 2-needle cannulation during month 3 post index procedure;
    - 5 subjects started 2-needle cannulation during month 4 post index procedure;
    - 3 subjects started 2-needle cannulation during month 6 post index procedure (all three subjects received vein superficialization/transposition);
    - 1 subject started 2-needle cannulation during month 7 post index procedure. This subject had 1-needle cannulation of the endoAVF beginning during month 4 post index procedure.
  - 2/21 subjects had fistula abandoned prior to cannulation start
- 2/21 subjects started cannulation of endoAVF with one needle in endoAVF and one needle CVC1/22 subjects received a kidney transplant on the 2nd week post index procedure

Out of 17 on-dialysis subjects who initiated dialysis utilizing 2-needle cannulation:

- 1/17 subject moved away (to a rural location) shortly after the endoAVF index procedure and started receiving healthcare through a non-study health authority. Subject came back to the study site for a 3-month follow up visit during which successful 2-needle cannulation via endoAVF was conducted.
- 16/17 subjects met the functional cannulation criteria.

<u>Supportive Clinical Data Set: Global Analysis</u>

Objective: The objective of the Global Analysis is to report and analyze data from multiple clinical studies and the commercial experience of the everlinQ® endoAVF system, individually by study and in the aggregate with pooled data. Aggregate effectiveness data is presented for all subjects; aggregate safety data is presented for the 6Fr cases alone. The Global Analysis was intended to supplement the NEAT Study data, including data to support a training program and labeling modifications.

Design:

<u>Prospective Study Data</u>

The FLEX, NEAT, EU PMCF and EASE studies were each prospectively planned and executed single-arm studies. Each study obtained the required institutional ethics approvals and all subjects provided informed consent prior to treatment. Data were collected via Case Report Forms and were independently monitored. Inclusion criteria required subjects to need vascular access for long-term hemodialysis with target vein diameter ≥ 2 mm, target artery diameter ≥ 2 mm, and ≤ 2 mm between target artery and vein. Relevant safety events were submitted for independent CEC adjudication. All procedural and post-procedural adverse events ("AEs") and secondary procedures were collected. Procedure success and patency effectiveness data were collected during the follow-up period: 6-month follow-up for FLEX and EASE and 12-month follow-up for NEAT and EU-PMCF.

Commercial Data

The Commercial data source was collected and reported by treating physicians from open-label commercial use of the 6Fr everlinQ® endoAVF System. The physician-reported data utilized a form generated by TVA based on the guidance of in-country regulatory counsel to specifically conform to applicable privacy regulations. The form was designed to specifically exclude any information that could be deemed to be personal data. AEs were submitted for CEC adjudication.

Patient Populations: A total of 236 subjects were available for analysis through the August 2017 cutoff date. Among these, 157 (66.5%) were in the four clinical studies and 79 (33.5%) were from the COMM study population.

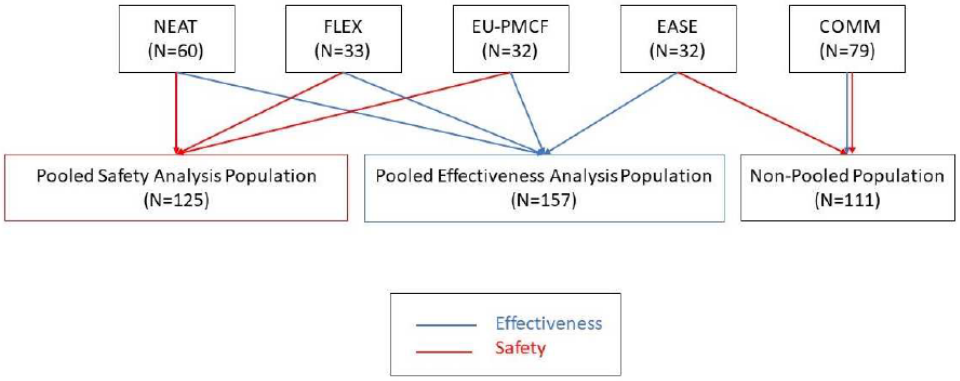


Figure 5: Safety and Effectiveness Data Available by Data Source

Analysis Endpoints:

Safety Endpoints

The safety endpoints are defined as the proportion of subjects with the following:

1. Serious adverse events (SAEs)
    - SAEs defined as adverse events that
        a. led to death,

b. led to serious deterioration in the health of the subject, that either resulted in 1) a life threatening injury, or 2) a permanent impairment of a body structure or a body function, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, or

c. led to foetal distress, foetal death or a congenital abnormality or birth defect

2. Significant events
    - Significant Events included device or procedure-related adverse events that either could be limb-threatening if not promptly identified or treated, or required additional therapy to reestablish patency of the endoAVF) access circuit, irrespective of whether they met the criteria for an SAE.
3. Device-related SAEs
4. Procedure-related SAEs
5. Brachial closure device-related SAEs
6. Embolization coil-related SAEs

Effectiveness Endpoints

The effectiveness endpoints of the Global Analysis were the following:

1. Procedure Success: The proportion of subjects who achieved successful endoAVF creation as confirmed by intraprocedural angiography/fistulogram or duplex ultrasound verification performed post-procedure. This definition corresponds to the term "Technical Success" commonly used in other studies.
2. Time to Cannulation: The interval of time from the index procedure to successful 2-needle cannulation of the endoAVF.
3. Cannulation Success: The proportion of subjects who achieved a successful cannulation of the endoAVF with 2-needles for dialysis. A subject may be called a 'cannulation success' with the first successful 2-needle cannulation of the endoAVF.
4. Primary Patency: The interval from the time of access placement until any intervention designed to maintain or reestablish patency, access thrombosis, access abandonment, or the time of measurement of patency (Society for Vascular Surgery Reporting Standards definition).
5. Modified Primary Patency: Identical to Primary Patency except that loss was also triggered by reinterventions not directly related to the access circuit; namely coiling or vessel ligation of venous outflow tributaries to encourage flow into the superficial, more easily accessible veins of the upper arm.
6. Assisted Primary Patency: The interval from access placement to thrombosis or abandonment; not triggered by access circuit interventions performed in the absence of occlusion.
7. Secondary Patency: The interval from the time of access placement until access abandonment, lost to thrombosis, or the time of patency measurement including intervening manipulations (surgical or endovascular interventions) designed to re-establish functionality in thrombosed access (SVS Reporting Standards definition).

8. Functional Patency: The interval of time from the first 2-needle dialysis utilizing the access until access abandonment (SVS Reporting Standards definition).
9. Functional Cannulation: Successful 2-needle access of the endoAVF access circuit with performance of more than 2/3rds of dialysis sessions of at least 120 minutes in duration over a continuous 28-day period. This measure was defined to more aptly measure whether an endoAVF resulted in a working access site for a subject, and is more pertinent to a subject, as opposed to Successful Cannulation, which is limited to completing a single successful 2-needle cannulation.

Eligibility Criteria Summary: The table below shows all of the criteria that were used to enroll subjects in the clinical studies. The "yes/no" answers indicate whether each criterion was evaluated for subject eligibility for the study in question. In general, the eligibility criteria for the studies were similar among the data sources. Inclusion criteria required subjects to need vascular access for long-term hemodialysis with target vein diameter ≥ 2 mm, target artery diameter ≥ 2 mm, and ≤ 2 mm between target artery and vein.

Table 18: Comparison of Eligibility Criteria Across Data Sources

	FLEX	NEAT	EU-PMCF	EASE
Geography	PY	CA, AU	DE, GB	PY
Size of System	6Fr	6Fr	6Fr	4Fr
Inclusion Criteria				
Eligible for AVF	Yes	Yes	Yes	Yes
Age	Yes	Yes	Yes	Yes
Kidney failure	Yes	Yes	Yes	Yes
Target AVF distance	Yes	Yes	No	No
Target vein diameter	Yes	Yes	Yes	Yes
Target artery diameter	Yes	Yes	Yes	Yes
Life Expectancy	Yes	Yes	Yes	Yes
Exclusion Criteria				
Informed Consent Required	Yes	Yes	Yes	Yes
Significant baseline conditions	Yes	Yes	Yes	Yes
Central vein stenosis > 50%	Yes	Yes	Yes	Yes
Hypercoagulable state	Yes	Yes	Yes	Yes
Planned/prior procedure < 30 days	Yes	Yes	Yes	Yes
Target vessel abnormality	Yes	Yes	Yes	Yes
Pregnancy	Yes	Yes	Yes	Yes
Known bleeding diathesis	Yes	Yes	Yes	Yes
Immunosuppression	Yes	Yes	Yes	Yes
Documented history of drug abuse	Yes	Yes	Yes	Yes
Body mass index	Yes	Yes	No	No
Contrast/Sedation/Anesthesia	No	Yes	Yes	Yes

PY- Paraguay, CA- Canada, AU- Australia, DE- Germany, GB- United Kingdom, AVF- Arteriovenous fistula

Data Quality Characteristics: Adverse events were assessed by an Independent Medical Monitor and an Independent Clinical Events Committee (CEC). Each event was classified with respect to:

1. Relationship to the study device
2. Relationship to the procedure
3. Relationship to coil embolization, if used
4. Relationship to a brachial artery closure device, if used
5. Whether the event was an Unanticipated Adverse Device Effect
6. Whether the event met the definition of a Significant Event

The determination of a Significant Event was made by the Medical Monitor as follows:

1. Yes, event was related to the study device or index procedure and could be limb-threatening if not promptly identified or treated

2. Yes, event was related to the study device or index procedure and additional therapy was required to re-establish an occluded AV access

3. No, neither of the above.

All procedural safety data and relevant post-procedure events were adjudicated by an independent CEC. The CEC Charter describes the event definitions, the adjudication process, and the CEC output data. The CEC consisted of three independent physicians with expertise in vascular surgery, interventional nephrology, and/or interventional radiology.

Study Quality Characteristics are shown in the table below:

Table 19: Comparison of Quality Characteristics Across Studies

	FLEX	NEAT	EU-PMCF	EASE
Geographies	PY	CA, AU	DE, GB	PY
Size of System	6Fr	6Fr	6Fr	4Fr
Adverse Event Source Collection	Yes	Yes	Yes	Yes
Statistical Analysis Plan	No	Yes	Yes	No
Monitoring Plan	Yes	Yes	Yes	Yes
Interim Monitoring	Yes	Yes	Yes	Yes
Data Management Plan	No	Yes	Yes	Yes
Database Validation Plan/Report	No	Yes	Yes	No
Data – Review for Completeness/Accuracy	Yes	Yes	Yes	Yes
Data - Query Generation/Resolution	Yes	Yes	Yes	Yes
Core Lab (Duplex Ultrasound)	No	Yes	Yes	No
Clinical Event Committee	Yes	Yes	Yes	Yes
Data Safety Monitoring Board	No	Yes	No	No
PY- Paraguay, CA- Canada, AU- Australia, DE- Germany, GB- United Kingdom				

Accountability: The protocol-specified follow-up duration was 12 months in the NEAT and EU-PMCF studies and 6 months in FLEX and EASE. Subjects were withdrawn when they exited a study due to abandonment of the endoAVF, successful renal transplantation, or if the subject withdrew consent voluntarily.

Of the 123 eligible subjects in the Pooled population 109 (88.6%) completed the 6 month follow-up visit. Of the 53 eligible subjects with pre-planned 12 month visits, 49 (92.5%) completed the 12 month visit.

Table 20: Study Accountability

Follow-Up Interval[1]	NEAT (N=60)	FLEX (N=33)	EU-PMCF[4] (N=32)	EASE (N=32)	Pooled[2] (N=157)
Follow-Up Duration	12 Months	6 Months	12 Months	6 Months	NA
Postoperative (0-10 Days):					
Eligible Subjects	60/60 (100.0%)	33/33 (100.0%)	32/32 (100.0%)	32/32 (100.0%)	157/157 (100.0%)
Death[5]	0/60 (0.0%)	1/33 (3.0%)	0/32 (0.0%)	0/32 (0.0%)	1/157 (0.6%)
Withdrawal[3]	1/60 (1.7%)	0/33 (0.0%)	5/32 (15.6%)	1/32 (3.1%)	7/157 (4.5%)
Visit Within Interval	58/60 (96.7%)	32/33 (97.0%)	25/32 (78.1%)	31/32 (96.9%)	146/157 (93.0%)
30-Days (11 – 45 Days)					
Eligible Subjects	59/60 (98.3%)	32/33 (97.0%)	26/32 (81.3%)	31/32 (96.9%)	148/157 (94.3%)
Death[5]	1/59 (1.7%)	2/32 (6.3%)	0/26 (0.0%)	1/31 (3.2%)	4/148 (2.5%)
Withdrawal[3]	0/59 (0.0%)	0/32 (0.0%)	2/26 (7.7%)	2/31 (6.5%)	4/148 (2.5%)
Visit Within Interval	57/59 (96.6%)	30/32 (93.8%)	22/26 (84.6%)	24/31 (77.4%)	133/148 (84.7%)
3-Months (46 – 135 Days)					
Eligible Subjects	58/60 (96.7%)	30/33 (90.9%)	24/32 (75.0%)	26/32 (81.3%)	138/157 (87.9%)
Death[5]	1/58 (1.7%)	1/30 (3.3%)	3/24 (12.5%)	3/26 (11.5%)	8/138 (5.8%)
Withdrawal[3]	2/58 (3.4%)	0/30 (0.0%)	3/24 (12.5%)	2/26 (7.7%)	7/138 (5.1%)
Visit Within Interval	55/58 (94.8%)	28/30 (93.3%)	18/24 (75.0%)	13/26 (50.0%)	114/138 (82.6%)
6-Months (136 – 270 Days)					
Eligible Subjects	55/60 (91.7%)	28/33 (84.8%)	18/32 (56.3%)	22/32 (68.8%)	123/157 (78.3%)
Death[5]	0/55 (0.0%)	0/28 (0.0%)	0/18 (0.0%)	1/22 (4.5%)	1/123 (0.8%)
Withdrawal[3]	2/55 (3.6%)	0/28 (0.0%)	0/18 (0.0%)	0/22 (0.0%)	2/123 (1.6%)
Visit Within Interval	53/55 (96.4%)	23/28 (82.1%)	11/18 (61.1%)	22/22 (100.0%)	109/123 (88.6%)
12-Months (271 – 390 Days)					
Eligible Subjects	53/60 (88.3%)	NA	NA[6]	NA	53/60 (88.3%)
Death[5]	1/53 (1.9%)	NA	NA	NA	1/53 (1.9%)
Withdrawal[3]	3/53 (5.7%)	NA	NA	NA	3/53 (5.7%)
Visit Within Interval	49/53 (92.5%)	NA	NA	NA	49/53 (92.5%)

1-The Follow-Up Intervals in this table are constructed to be contiguous and standardized between the studies evaluated. They do not correspond to prespecified windows in each of the individual study protocols (follow-up windows were specified in the NEAT study protocol alone), nor do they correspond to the windows used to standardize follow-up for the Global Analysis.

2-Pooled studies include all data sources except COMM (commercial cases).

3-Withdrawn subjects include those subjects who exited the study due to lack of procedure success, endoAVF abandoned, transplant, or withdrew consent.

4-NEAT, FLEX, and EASE are completed studies. EU-PMCF is ongoing, with active enrollment and follow-up.

5- No EU-PMCF subjects had 12-month interval (beginning at day 271) data reported at the time of the data snap.

Demographics: Demographics for the Pooled population and each individual study population is provided in the table below. Males (65%) were more common than females (35%). The mean age was 57 in the pooled data set. There was a predominance of Caucasian subjects in the European/Canadian studies (NEAT and EU-PMCF). The FLEX and EASE studies were uniformly comprised of subjects of Hispanic ethnicity because the studies were conducted in Paraguay. A small number of Asian and Indian subjects were enrolled. No Black subjects were enrolled in any of the studies. No demographic data or baseline characteristics were collected for the commercial cases.

Table 21: Summary of Study Demographics

Characteristic	NEAT (N=60)	FLEX (N=33)	EU-PMCF (N=32)	EASE (N=32)	Pooled (N=157)	COMM (N=79)
Gender:						
Male	39/60 (65.0%)	20/33 (60.6%)	21/32 (65.6%)	31/32 (96.9%)	111/157 (70.7%)	NA
Female	21/60 (35.0%)	13/33 (39.4%)	11/32 (34.4%)	1/32 (3.1%)	46/157 (29.3%)	NA
Age:						
Mean ± SD	59.9 ± 13.6	51.0 ± 11.4	63.5 ± 12.7	50.9 ± 12.9	57.0 ± 13.8	NA
Race:						
Caucasian	36/60 (60.0%)	NA	27/32 (84.4%)	0/32 (0.0%)	63/124 (50.8%)	NA
Black	0/60 (0.0%)	NA	0/32 (0.0%)	0/32 (0.0%)	0/124 (0.0%)	NA
Asian	4/60 (6.7%)	NA	4/32 (12.5%)	0/32 (0.0%)	8/124 (6.5%)	NA
Indian	15/60 (25.0%)	NA	1/32 (3.1%)	NA	16/124 (12.9%)	NA
Ethnicity:						
Not Hispanic/Latino	58/60 (96.7%)	0/33 (0.0%)	32/32 (100.0%)	0/32 (0.0%)	90/157 (57.3%)	NA
Hispanic or Latino	2/60 (1.7%)	33/33 (100.0%)	0/32 (0.0%)	32/32 (100.0%)	67/157 (42.7%)	NA
Height (cm) :						
Mean ± SD	169.5 ± 11.7	165.0 ± 8.3	165.8 ± 10.6	170.4 ± 9.6	168.0 ± 10.6	NA
Weight (kg) :						
Mean ± SD	80.9 ± 21.9	65.8 ± 10.3	81.7 ± 18.5	75.6 ± 13.0	76.8 ± 18.5	NA
BMI:						
Mean ± SD	27.9 ± 6.1	24.2 ± 3.9	29.8 ± 6.8	25.9 ± 3.1	27.1 ± 5.7	NA
Systolic BP:						
Mean ± SD	144.5 ± 22.5	NA	137.7 ± 20.3	163.5 ± 26.0	149.7 ± 25.9	NA

Diastolic BP:						
Mean ± SD	83.4 ± 12.5	NA	72.5 ± 9.2	99.8 ± 18.8	85.8 ± 19.0	83.4 ± 12.5
Target Vein Diameter (mm):						
Mean ± SD	2.5±0.5	NA	3.1±0.8	2.7±0.8	2.7±0.7	NA
Target Artery Diameter (mm):						
Mean ± SD	3.8±0.8	NA	3.7±0.6	3.0±0.7	3.6±0.8	NA
The denominator for each data point varies due to exclusion of subjects with missing data. *NA means data not collected*						

Results:

Procedural Characteristics

The endoAVF was created on the right side in one-third of subjects and on the left side in two-thirds of subjects. The target vein diameter as determined by pre-procedure duplex ultrasonography averaged 2.7 ± 0.7 mm. The target artery diameter, also determined on the pre-procedure duplex ultrasound, averaged 3.6 ± 0.8 mm.

The endoAVF was created between the ulnar artery and vein in all studies except EASE, where radio-radial endoAVF were created in 62.5% of the subjects and ulnar-ulnar endoAVFs were performed in the remaining 37.5%. The site of arterial access was, by and large, dictated by the size of the system. The 6Fr systems used in all studies except EASE mandated brachial artery and brachial vein access. The 4Fr system used in EASE facilitated access from the radial (59.4%) and ulnar (12.5%) arteries in addition to the brachial artery (28.1%). Venous access was brachial for all subjects except those in EASE. Closure of the arterial access site was with manual compression in 63.7% of subjects, while a brachial access closure device was used in 36.3% of the pooled population.

Adjunctive Procedures

Adjunctive procedures performed at the index procedure included planned coiling of outflow veins and the use of a brachial closure device. Unplanned procedures included balloon angioplasty or stenting of stenotic vessels. The frequency of these procedures appears in Table 22 below.

The most common adjunctive procedure was therapeutic coil embolization which occurred during the index procedure in 123/157 (78.3%) of the Pooled Effectiveness Population.

Table 22: Adjunctive Procedures at the Time of Index Procedure

Adjunctive Procedures	NEAT	FLEX	EU-PMCF	EASE	Pooled Studies	COMM
Therapeutic Embolization	56	17	27	19	119	59
Closure Device	41	NA	2	2	45	11
PTA	0	0	0	0	0	0
Stent	0	0	0	0	0	0
Other*	6	1	2	0	9	1
Subjects with ≥1 Procedure	58/60 (96.7%)	18/33 (54.5%)	27/32 (84.4%)	20/32 (62.5%)	123/157 (78.3%)	60/79 (75.9%)

The Pooled Studies in this table include the NEAT, FLEX, EU-PMCF, and EASE studies.

Adjunctive procedures are tabulated by the procedure (i.e. one subject may have more than one adjunctive procedure), except for the last row which tabulated the data at the subject level.

**Other procedures include thrombolysis (1) thrombectomy (2), new surgical AVF (1), open surgical repair for an intraoperative complication (6)*

Independent Medical Monitor classified data.

Safety Endpoints

The Global Analysis of the everlinQ® System data is summarized in Table 23 below. For each outcome, the data represents the number of subjects experiencing an event divided by the number of subjects in the study. The Pooled Safety Population included subjects treated in the FLEX, EU-PMCF and NEAT studies (6Fr system) (N=125), but did not include subjects in the EASE study (4Fr system) or in the Commercial (COMM) cohort. All safety events were adjudicated by the CEC.

Table 23 below provides safety outcomes for the pooled 6Fr data (FLEX, EU-PMCF, NEAT) and 4Fr data (EASE). In the Pooled Safety population 15/125 (12.0%) subjects reported an unrelated SAE as adjudicated by the CEC. In total, 15/125 (12.0%) subjects reported an SAE that was related to the device and/or procedure. 4/125 (3.2%) subjects reported a device-related SAE, and 15/125 (12.0%) reported a procedure-related SAE.

Closure device-related SAEs occurred in 4.8% of the population (6/125). There were no coil-related SAEs (0/125). There were 8 deaths included as SAEs in the Pooled Safety Population and all were unrelated to the study procedure or device (6.4%, 8/125). Commercial data from outside the US did not indicate any new or different types of risks.

Table 23: Safety Endpoint Results – Global Analysis

	NEAT (N=60)	FLEX (N=33)	EU-PMCF (N=32)	EASE (N=32)	Pooled* (Safety=125)	COMM (N=79)
Safety Endpoints						
SAE-unrelated	9/60 (15.0%)	4/33 (12.1%)	1/32 (3.1%)	6/32 (18.7%)	15/125 (12.0%)	0/79 (0%)
SAE-related	5/60 (8.3%)	4/33 (12.1%)	6/32 (18.7%)	1/32 (3.1%)	15/125 (12.0%)	3/79 (3.8%)
Device-Related SAE	1/60 (1.7%)	1/33 (3.0%)	2/32 (6.3%)	0/32 (0.0%)	4/125 (3.2%)	1/79 (1.3%)
Procedure-Related SAE	5/60 (8.3%)	4/33 (12.1%)	6/32 (18.8%)	1/32 (3.1%)	15/125 (12.0%)	3/79 (3.8%)
Closure Device-Related SAE	4/60 (6.7%)	0/33 (0.0%)	2/32 (6.3%)	0/32 (0.0%)	6/125 (4.8%)	0/79 (0.0%)
Coil-Related SAE	0/60 (0.0%)	0/33 (0.0%)	0/32 (0.0%)	0/32 (0.0%)	0/125 (0.0%)	0/79 (0.0%)

This summary table is intended to provide standalone results for the most important safety study endpoints.

The Pooled Safety Population includes NEAT, FLEX, and EU-PMCF.

The 6- and 12-month windows are defined as 180 and 360 days ± 30 days, respectively. The data in this table represent events through the end of the respective windows; i.e. 210 days for 6 months and 390 days for 12 months.

The safety endpoints are tabulated on a per-subject basis and represent the number of subjects who experienced at least one event of the specified category over the duration follow-up.

SAE- Serious Adverse Event as adjudicated by the CEC, reported at any time during follow-up.

NA- Not applicable. Indicates that the data point is beyond the length of follow-up for a study or that the number of evaluable subjects is zero at that time point.

Significant Events included device or procedure-related adverse events that either a) could be limb-threatening if not promptly identified or treated, or b) required additional therapy to reestablish patency of the endoAVF access circuit, irrespective of whether they met the criteria for an SAE.

Data is site-reported, with independent Medical Monitor classifications and CEC-adjudicated data

**For all safety endpoints, pooled studies include NEAT, FLEX, and EU-PMCF, and reflect all data from each study.*

The 6- and 12-month timepoints were calculated at the end of the follow-up windows, through 210 and 390 days, respectively.

Safety Events After Training

After completion of the NEAT Study, a training program was implemented to instruct physicians on the proper use of the device, recommended techniques, potential complications, and other information. The training includes diagrams, videos, training models, and proctored cases. The training also includes instruction on how to achieve hemostasis at the brachial artery access site using manual compression instead of using vascular closure devices.

Among the 20 subjects evaluated in the EU-PMCF study and commercial cases after implementation of the training program, all subjects achieved hemostasis after the procedure with manual compression of the brachial artery access site, and no subjects experienced serious adverse events as shown in Table 24 below. Although this demonstrates a numerical reduction in

the rate of serious adverse events, the data was collected in a limited number of subjects and no conclusions can be drawn regarding whether or not this is a statistically significant difference.

Table 24: SAEs by Training Status (CEC-Adjudicated)

Training Status	Statistics	NEAT (N=60)	FLEX (N=33)	EU-PMCF (N=32)	COMM (N=78) *
Procedural (<72 hours)					
Pre-Training	n/N (%)	5/60 (8.3%)	2/33 (6.1%)	5/21(23.8%)	3/69(4.4%)
Post-Training	n/N (%)	NA	NA	0/11 (0.0%)	0/9 (0.0%)
Procedural (>72 hours, <-30 days)					
Pre-Training	n/N (%)	2/60 (3.3%)	2/33 (6.06%)	2/21 (9.52%)	0/69 (0.0%)
Post-Training	n/N (%)	NA	NA	0/11 (0.0%)	0/9 (0.0%)
Follow-Up (>30 days)					
Pre-Training	n/N (%)	10/60 (16.6%)	4/33(12.1%)	1/21(4.8%)	0/69 (0.0%)
Post-Training	n/N (%)	NA	NA	0/11 (0.0%)	0/9 (0.0%)
Any Timepoint					
Pre-Training	n/N (%)	15/60 (25.0%)	8/33(24.24%)	7/21(33.3%)	3/69 (4.4%)
Post-Training	n/N (%)	NA	NA	0/11 (0.0%)	0/9 (0.0%)

** Procedure date unavailable for 1 COMM subject*
CEC-adjudicated data

Effectiveness Endpoints

A summary of the Effectiveness outcomes is tabulated in the main summary table (Table 25) below. The Pooled Effectiveness Population comprised subjects treated as part of the FLEX, EU-PMCF, NEAT, and EASE studies (N=157). Subjects treated commercially were not included in this population.

Procedural success, defined as the successful creation of an endoAVF with blood flow confirmed intraoperatively by fistulography or by duplex ultrasound postoperatively, was achieved in 96.8% (152/157) of the Pooled Effectiveness Population. Cannulation Success (2-needle access and hemodialysis through the fistula) was achieved in 82.4% of subjects through the 6 month window and in 92.4% of subjects through the 12 month window after the index procedure.

The median time to successful cannulation was 2.1 months after a subject went on dialysis (or after the index procedure in those that were on dialysis at enrollment). The Kaplan-Meier estimate for Functional Cannulation (All Subjects), defined in the table below, was 42.4% at 6 months and 58.9% at 12 months. For patients already on dialysis at the time of enrollment, Functional Cannulation was 56.1% and 78.4% at 6 and 12 months, respectively. The reported Kaplan-Meier estimate of Primary Patency was 82.7% and 74.8% at 6 and 12 months, respectively. Similar results were observed in the commercial cases, where the corresponding data was available.

Table 25: Effectiveness Endpoint Results

	NEAT (N=60)	FLEX (N=33)	EU-PMCF (N=32)	EASE (N=32)	Pooled* (Effectiveness=157)	COMM (N=45)
Effectiveness Endpoints:						
Procedural Success	59/60 (98.3%)	32/33 (97.0%)	29/32 (90.6%)	32/32 (100.0%)	152/157 (96.8%)	44/45 (97.8%)
Time to Cannulation (Months)						
Observations	31	25	11	21	88	18
Median [IQR]	3.1 [2.7,5.6]	2.1 [1.9,2.4]	2.4 [1.4,3.4]	1.3 [1.1,1.6]	2.1 [1.6,3.2]	1.7 [0.4,2.9]
Mean ± SD	4.1 ± 2.3	2.2 ± 0.8	3.0 ± 1.9	1.4 ± 0.5	2.8 ± 1.9	2.3 ± 2.3
(Min, Max)	(1.4, 10.7)	(1.1, 4.6)	(1.2, 7.2)	(1.0, 3.0)	(1.0, 10.7)	(0.3, 7.8)
Cannulation Success, 6-Month	70.6% (±7.4%)	100.0% (±0.0%)	71.2% (±13.3%)	90.4% (±6.4%)	82.4% (±4.0%)	94.3% (±5.5%)
Cannulation Success, 12-Month	86.1% (±6.6%)	NA	100.0% (±0.0%)	NA	92.4% (±3.6%)	100.0% (±0.0%)
Functional Cannulation, 6-Month	36.3% (±6.7%)	88.6% (±7.0%)	63.2% (±13.6%)	85.8% (±7.5%)	42.4% (±6.1%)	NA
Functional Cannulation, 12-Month	53.1% (±7.4%)	NA	100.0% (±0.0%)	NA	58.9% (±6.6%)	NA
Functional Cannulation, Dialysis Subset, 6-Month†	50.4% (±8.2%)	94.5% (±5.1%)	71.1% (±13.3%)	85.8% (±7.5%)	56.1% (±7.1%)	NA
Functional Cannulation, Dialysis Subset, 12-Month†	74.2% (±7.0%)	NA	NA	NA	78.4% (±6.7%)	NA
Primary Patency, 6-Month	81.1% (±5.1%)	96.4% (±3.5%)	78.9% (±7.7%)	83.3% (±6.8%)	82.7% (±3.5%)	71.3% (±7.4%)
Primary Patency, 12-Month	73.4% (±5.9%)	N/A	78.9% (±7.7%)	N/A	74.8% (±4.9%)	63.5% (±8.4%)
Mod Primary Patency, 6-Month	76.5% (±5.5%)	53.6% (±9.4%)	68.4% (±8.8%)	83.3% (±6.8%)	70.5% (±4.0%)	71.3% (±7.4%)
Mod Primary Patency, 12-Month	61.1% (±8.1%)	N/A	68.4% (±8.8%)	N/A	56.3% (±7.1%)	63.5% (±8.4%)
Assist Prim Patency, 6-Month	84.8% (±4.7%)	96.4% (±3.5%)	82.1% (±7.3%)	86.8% (±6.2%)	85.8% (±3.2%)	71.3% (±7.4%)
Assist Prim Patency, 12-Month	77.2% (±5.6%)	N/A	82.1% (±7.3%)	N/A	78.2% (±4.7%)	63.5% (±8.4%)
Secondary Patency, 6-Month	86.4% (±4.5%)	96.4% (±3.5%)	82.1% (±7.3%)	86.8% (±6.2%)	86.5% (±3.1%)	70.4% (±7.5%)

Secondary Patency, 12-Month	78.9% (±5.4%)	N/A	82.1% (±7.3%)	N/A	79.0% (±4.6%)	62.8% (±8.4%)
Functional Patency, 6-Month	96.3% (±3.6%)	100.0% (±0.0%)	100.0% (±0.0%)	100.0% (±0.0%)	98.1% (±1.8%)	95.0% (±4.9%)
Functional Patency, 12-Month	96.3% (±3.6%)	N/A	100.0% (±0.0%)	N/A	98.1% (±1.8%)	82.3% (±9.3%)

This summary table is intended to provide standalone results for the most important efficacy study endpoints.

The Pooled Effectiveness Population includes those studies plus EASE. The exception is Functional Cannulation, where the pooled dataset is limited to NEAT and EU-PMCF since more extensive cannulation data was available in those studies.

The 6- and 12-month windows are defined as 180 and 360 days ± 30 days, respectively. The data in this table represent events through the end of the respective windows; i.e. 210 days for 6 months and 390 days for 12 months.

NA- Not applicable. Indicates that the data point is beyond the length of follow-up for a study or that the number of evaluable subjects is zero at that time point.

Procedural Success was defined as successful endoAVF creation confirmed via intraprocedural fistulography or by duplex ultrasound performed post-procedure.

Time to Cannulation is the time between the index procedure to the first successful endoAVF cannulation. Cannulation Success was defined as successful 2-needle cannulation and dialysis through the endoAVF.

Functional Cannulation is defined as 2-needle access of the endoAVF access circuit with performance of ≥ 2/3rds of ≥ 120-minute dialysis sessions through the endoAVF access circuit over a continuous 28-day period. Functional Cannulation is expressed as the Kaplan-Meier estimate (Standard Error).

Patency definitions are from the Society of Vascular Surgery Reporting Standards document; Sidawy et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses, J Vasc Surg 2002;35:603-10. Primary patency is the interval of time of access placement until any intervention designed to maintain or re-establish patency, access thrombosis, access abandonment, or the time of measurement of patency. Assisted Primary Patency is the interval from access placement to thrombosis or abandonment; not triggered by access circuit interventions performed in the absence of occlusion. Secondary patency is the interval of time of access placement until access abandonment, lost to thrombosis, or the time of patency measurement including intervening manipulations (surgical or endovascular interventions) designed to re-establish functionality in thrombosed access. Functional patency is the interval of time from the first 2-needle dialysis utilizing the access until access abandonment.

Patency rates are expressed as Kaplan-Meier estimates (Standard Error)

Data is site-reported, with independent Medical Monitor classifications and CEC-adjudicated data

** For all effectiveness endpoints except Functional Cannulation, pooled studies include NEAT, FLEX, EU-PMCF, and EASE. The pooled studies for Functional Cannulation excluded FLEX and EASE, since the extent of available cannulation data was less than for the NEAT and EU-PMCF studies.*

†Functional Cannulation, specified in the dialysis subset defined as the cohort of subjects who were enrolled on dialysis or eventually went on dialysis during follow-up. The data include the NEAT and EU-PMCF studies alone.

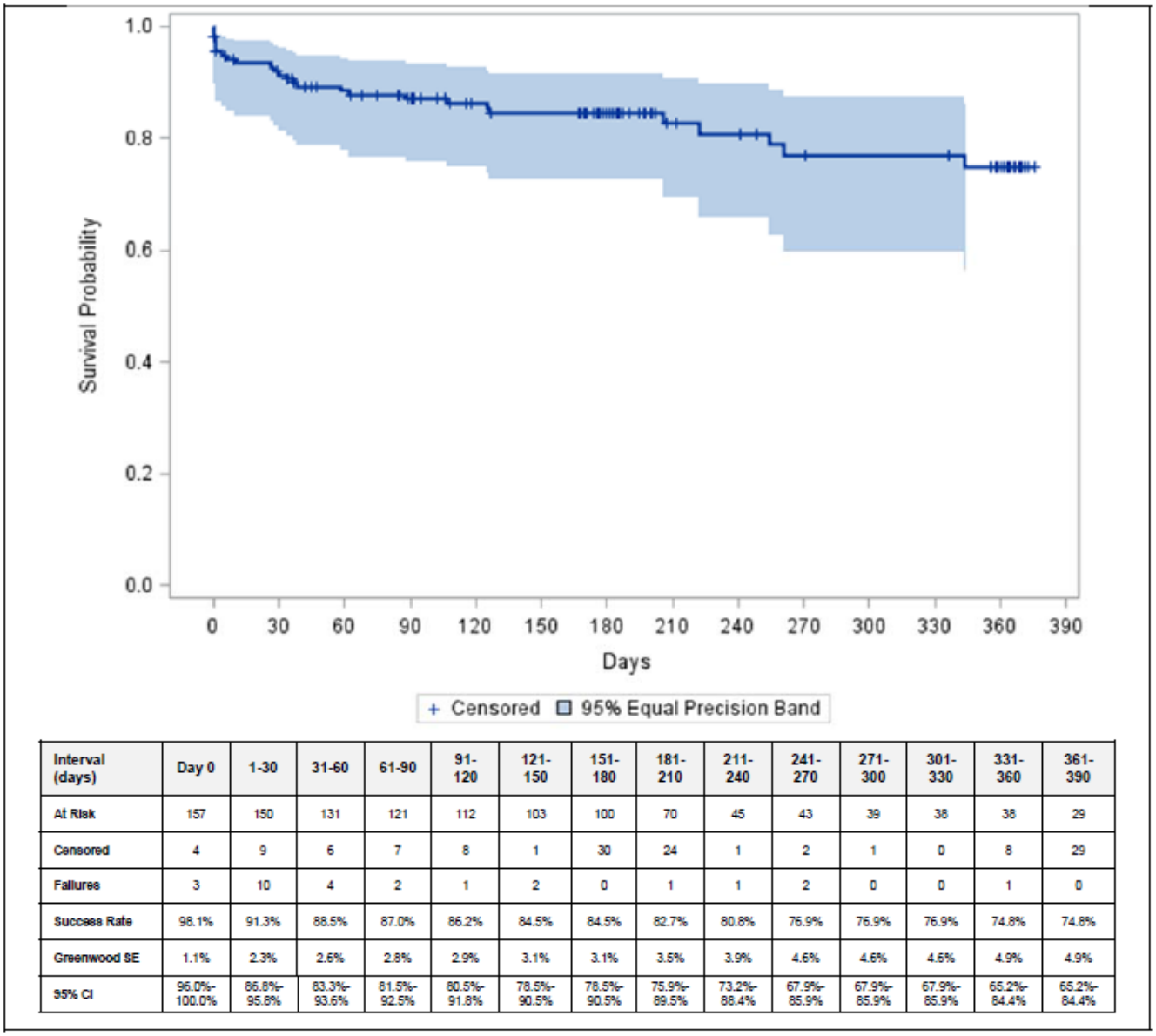
The 6- and 12-month timepoints were calculated at the end of the follow-up windows, through 210 and 390 days, respectively.

Patency Results

As shown in Table 25 above, the 6-month primary patency rates among the EU-PMCF (78.9%) and EASE (83.3%) studies were numerically similar to the 6-month primary patency rate in the NEAT study (81.1%). Among the entire pooled effectiveness population, the 6-month primary patency rate was 82.7%.

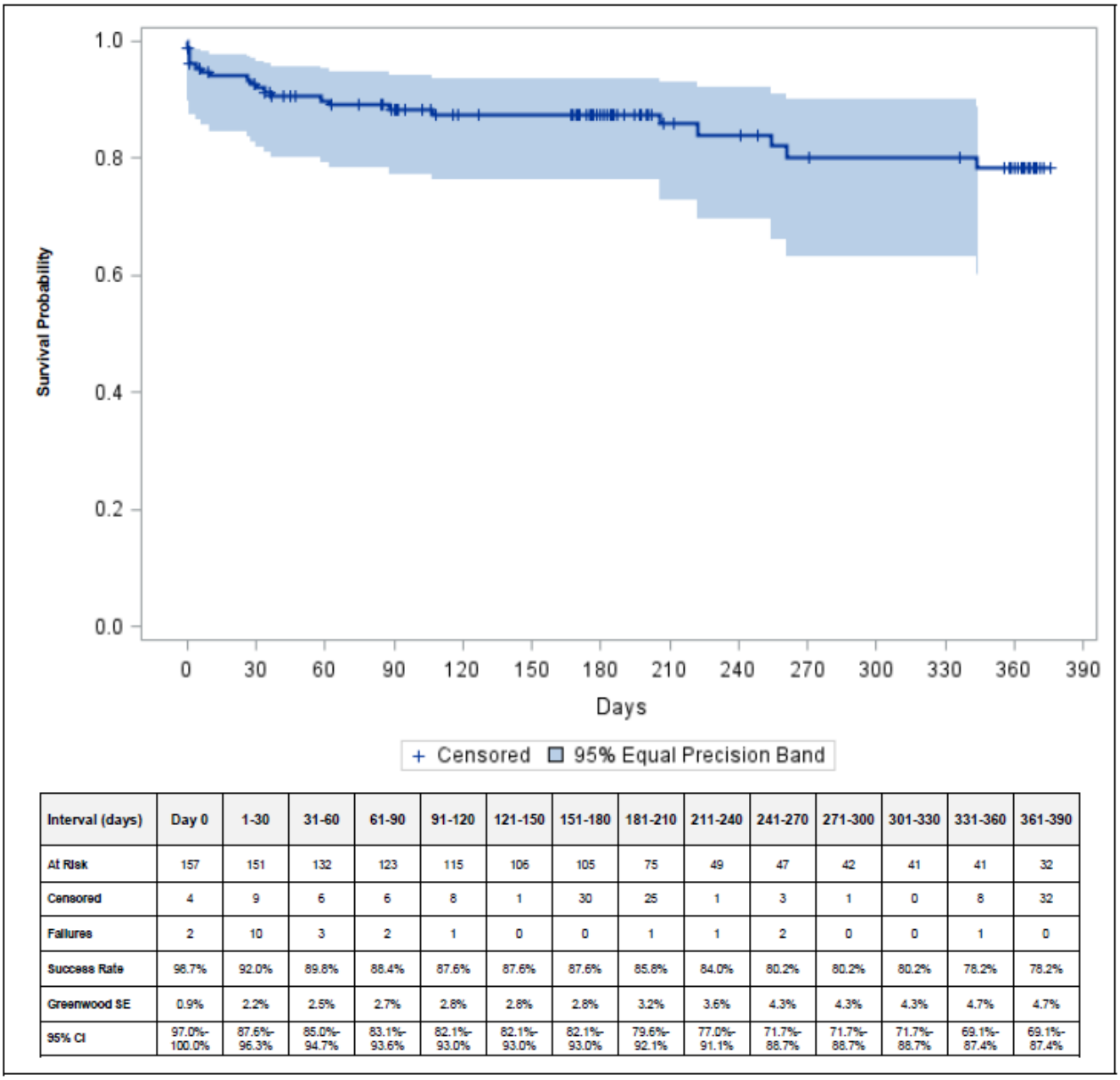
The figures below show patency rates for the pooled effectiveness population expressed as Kaplan-Meier estimates with shaded regions showing the 95% confidence interval. The 12-

month primary patency rate for the pooled effectiveness population was 74.8%, although only 29 subjects were evaluable at this 12 months as shown by the corresponding life table.



Interval (days)	Day 0	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	301-330	331-360	361-390
At Risk	157	150	131	121	112	103	100	70	45	43	39	38	38	29
Censored	4	9	6	7	8	1	30	24	1	2	1	0	8	29
Failures	3	10	4	2	1	2	0	1	1	2	0	0	1	0
Success Rate	98.1%	91.3%	88.5%	87.0%	86.2%	84.5%	84.5%	82.7%	80.8%	76.9%	76.9%	76.9%	74.8%	74.8%
Greenwood SE	1.1%	2.3%	2.6%	2.8%	2.9%	3.1%	3.1%	3.5%	3.9%	4.6%	4.6%	4.6%	4.9%	4.9%
95% CI	96.0%-100.0%	86.8%-95.8%	83.3%-93.6%	81.5%-92.5%	80.5%-91.8%	78.5%-90.5%	78.5%-90.5%	75.9%-89.5%	73.2%-88.4%	67.9%-85.9%	67.9%-85.9%	67.9%-85.9%	65.2%-84.4%	65.2%-84.4%

Figure 6: Primary Patency, Pooled Effectiveness Population



Interval (days)	Day 0	1-30	31-60	61-90	91-120	121-150	151-180	181-210	211-240	241-270	271-300	301-330	331-360	361-390
At Risk	157	151	132	123	115	106	105	75	49	47	42	41	41	32
Censored	4	9	6	6	8	1	30	25	1	3	1	0	8	32
Failures	2	10	3	2	1	0	0	1	1	2	0	0	1	0
Success Rate	98.7%	92.0%	89.6%	88.4%	87.6%	87.6%	87.6%	85.6%	84.0%	80.2%	80.2%	80.2%	78.2%	78.2%
Greenwood SE	0.9%	2.2%	2.5%	2.7%	2.8%	2.8%	2.8%	3.2%	3.6%	4.3%	4.3%	4.3%	4.7%	4.7%
95% CI	97.0%-100.0%	87.6%-96.3%	85.0%-94.7%	83.1%-93.6%	82.1%-93.0%	82.1%-93.0%	82.1%-93.0%	79.6%-92.1%	77.0%-91.1%	71.7%-88.7%	71.7%-88.7%	71.7%-88.7%	69.1%-87.4%	69.1%-87.4%

Figure 7: Assisted Primary Patency, Pooled Effectiveness Population

Functional Cannulation

Functional Cannulation is defined as successful 2-needle cannulations with at least 2 hours of hemodialysis through the access circuit, for two-thirds or more of the dialysis sessions in any continuous 28-day period. The time to Functional Cannulation is the duration from the index procedure to the start of the 28-day period.

Table 26 below shows the proportion of subjects in each category who had achieved functional cannulation at each timepoint. Additionally, the table shows the number of subjects who were evaluable in each category (N), as well as the median (months), mean ± SD (months), and range

of months subjects required to reach the 28-day period when they achieved Functional Cannulation success. The data come from the NEAT and EU-PMCF studies, as these studies used detailed cannulation logs.

Table 26: Functional Cannulation, Subjects Requiring Dialysis

Measure	On dialysis at enrollment	Pre-dialysis at enrollment who eventually went on dialysis	On dialysis at enrollment or pre-dialysis at enrollment who eventually went on dialysis
Functional Cannulation, 6-Month*	59.4% (±9.3%)	52.5% (±10.8%)	56.1% (±7.1%)
Functional Cannulation, 12-Month*	73.9% (±9.1%)	85.1% (±9.1%)	78.4% (±6.6%)
N	40	26	66
Median [IQR]	0.7 [0.0,3.5]	3.5 [1.9,7.4]	3.4 [2.1,7.2]
Mean ± SD	2.1 ± 2.6	5.0 ± 3.6	4.7 ± 3.7
Range (min, max)	(0.0, 9.5)	(0.3, 12.1)	(0.0, 12.4)
The 6- and 12-Month windows end at 210 and 390 days, respectively.			

Table 27 below shows the number of subjects who were evaluable for functional cannulation success from each data source; i.e., the number of subjects who initiated hemodialysis during each study. It also shows the percentage of subjects from each study who were on hemodialysis and achieved functional cannulation success at 6 months and 12 months, as well as the time to achieve functional cannulation success broken out by subjects who were on dialysis at enrollment and subjects who were pre-dialysis at the beginning of the study and eventually required hemodialysis.

Among the Pooled functional cannulation population – which includes only subjects from the NEAT and EU-PMCF studies because only these studies contained detailed cannulation logs – the functional cannulation success was 56.1% at 6 months and 78.4% at 12 months. Among these subjects, the average time to achieve functional cannulation success was 2.1 months for subjects who were on dialysis at enrollment and 5.0 months for subjects who were pre-dialysis at the time of study enrollment.

Table 27: Functional Cannulation Success* by Data Source

Metric	NEAT	FLEX	EU-PMCF	EASE	Pooled
Total N	60	33	32	32	92
Exited study predialysis	17	2	9	0	26
Total included in analysis	43	31	23	32	66
Functional Cannulation Success 6-Month+	50.4% CI[34.3% - 66.5%]	94.5% CI[84.5% - 100%]	71.1% CI[45.1%-97.1%]	85.8% CI[71.1%-100%]	56.1% CI[42.2%-69.9%]
Functional Cannulation Success 12-Month+	74.2% [58.7%-89.6%]	NA	NA	NA	78.4% CI[65.3%-91.4%]
Time to Cannulation (months)	Dialysis 3.9 ± 1.5 Predialysis 4.2 ± 3.0	Dialysis 2.2 ± 0.8 Predialysis NA	Dialysis 3.1 ± 1.4 Predialysis 2.9 ± 2.5	Dialysis 1.4 ± 0.5 Predialysis NA	Dialysis 2.1 ± 2.6 Predialysis 5.0 ± 3.6

*Excludes predialysis patients that never were on to dialysis through study exit
Pooled includes NEAT and EU-PMCF only as these studies contained detailed cannulation logs.
+ The 6- and 12-month windows end at 210 and 390 days, respectively

Conclusions: The NEAT Study and the Global Analysis demonstrated that there is a reasonable assurance of safety and effectiveness that the everlinQ® endoAVF System creates an arteriovenous fistula that can mature as a method of vascular access for hemodialysis. In the NEAT Study, a fistula was successfully created in 59/60 (98.3%) subjects and 52/60 (86.7%) met the primary endpoint success criteria for fistula maturation at 90 days. The rate of SAEs related to the device and/or procedure through 12 months was 8 SAEs in 5/60 subjects (8.3%), and the primary safety endpoint was met. Although 2 of the SAEs in the NEAT Study were related to vascular closure device embolization, safety data collected from the EU-PMCF and commercial cases after the implementation of a training program showed that all subjects (20/20) achieved hemostasis by manual compression of the brachial artery instead of using vascular closure devices, and no subjects (0/20 = 0%) experienced any SAEs after the implementation of the training program, as summarized in Table 24 above. Among NEAT Study subjects who went on hemodialysis during the study, the functional cannulation endpoint was met by 50.4% of subjects at 6 months and by 74.2% of subjects at 12 months. In the NEAT Study, the reported Kaplan-Meier estimate for primary patency was 81.1% at 6 months and 73.4% at 12 months. The reported Kaplan-Meier estimate for assisted primary patency at 12 months was 77.2%. In the NEAT Study, 56/60 subjects (93.3%) required the implantation of at least one embolization coil in their brachial vein at the time of the index procedure, with an average of 1.6 coils. After the index procedure, 17/60 subjects (28.3%) required at least one reintervention, with a total of 20 reinterventions among those 17 subjects.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

POSTMARKET EVALUATION

A postmarket evaluation will be conducted to collect data on the safety and effectiveness of the everlinQ® endoAVF System in U.S. patients. This is a postmarket, prospective, multi-center study of U.S. patients with chronic kidney disease who need hemodialysis and are candidates for the creation of an arteriovenous fistula with the everlinQ® endoAVF System. Safety and effectiveness data will be collected and compared to the pivotal study data that supported this De Novo application.

LABELING

The everlinQ® endoAVF System labeling consists of Instructions for Use and packaging labels. The Instructions for Use include the indications for use; a description of the device, contraindications, warnings, precautions; a list of commercially available electrosurgical devices that are compatible with the device; a detailed summary of the clinical data collected in support of the device; a list of potential adverse events; a shelf life; the expertise needed for the safe use of the device; and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

Please see the Limitations section above for important contraindications, warnings and precautions presented in the device labeling.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of a percutaneous catheter for creation of an arteriovenous fistula for hemodialysis access and the measures necessary to mitigate these risks.

Table 28: Identified Risks to Health and Mitigation Measures

Identified Risks to Health	**Mitigation Measures**
Unintended vascular or tissue injury	Non-clinical performance testing Animal testing Clinical performance testing Labeling
Adverse hemodynamic effects	Non-clinical performance testing Animal testing Clinical performance testing Labeling
Failure to create a durable fistula that is usable for hemodialysis	Animal testing Clinical performance testing
Use of the device adversely impacts future vascular access sites	Clinical performance testing Labeling
Adverse tissue reaction	Biocompatibility evaluation Labeling
Infection	Sterilization validation

	Shelf life testing Labeling
Electrical malfunction or interference leading to electrical shock, device failure, or inappropriate activation	Non-clinical performance testing Electrical safety testing Electromagnetic compatibility (EMC) testing
Software malfunction leading to device failure or inappropriate activation	Software verification, validation, and hazard analysis

SPECIAL CONTROLS:

In combination with the general controls of the FD&C Act, the percutaneous catheter for creation of an arteriovenous fistula for hemodialysis access is subject to the following special controls:

1. Clinical performance testing must evaluate:
    a. The ability to safely deliver, deploy, and remove the device;
    b. The ability of the device to create an arteriovenous fistula;
    c. The ability of the arteriovenous fistula to attain a blood flow rate and diameter suitable for hemodialysis;
    d. The ability of the fistula to be used for vascular access for hemodialysis;
    e. The patency of the fistula; and
    f. The rates and types of all adverse events.

2. Animal testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be assessed:
    a. Delivery, deployment, and retrieval of the device;
    b. Compatibility with other devices labeled for use with the device;
    c. Patency of the fistula;
    d. Characterization of blood flow at the time of the fistula creation procedure and at chronic follow-up; and
    e. Gross pathology and histopathology assessing vascular injury and downstream embolization.

3. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
    a. Simulated-use testing in a clinically relevant bench anatomic model to assess the delivery, deployment, activation, and retrieval of the device;
    b. Tensile strengths of joints and components;
    c. Accurate positioning and alignment of the device to achieve fistula creation; and
    d. Characterization and verification of all dimensions.

4. Electrical performance, electrical safety, and electromagnetic compatibility (EMC) testing must be performed for devices with electrical components.

5. Software verification, validation, and hazard analysis must be performed for devices that use software.

6. All patient-contacting components of the device must be demonstrated to be biocompatible.

7. Performance data must demonstrate the sterility of the device components intended to be provided sterile.

8. Performance data must support the shelf life of the device by demonstrating continued sterility, package integrity, and device functionality over the identified shelf life.

9. Labeling for the device must include:
    a. Instructions for use;
    b. Identification of system components and compatible devices;
    c. Expertise needed for the safe use of the device;
    d. A detailed summary of the clinical testing conducted and the patient population studied; and
    e. A shelf life and storage conditions.

BENEFIT/RISK DETERMINATION

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in the clinical studies described above. Types of harmful events include access site complications, pseudoaneurysm, thrombosis, closure device embolization, brachial artery dissection, hematoma, bruising, steal, swelling and pain. Among the NEAT study population described in the clinical data section above, the rate of serious device- and/or procedure-related harmful events was 5/60 (8.3%) and the rate of non-serious device- and/or procedure-related harmful events was 22/60 (36.7%). There were no deaths adjudicated as related to the device or procedure. A total of 9 occlusion and/or thrombosis events were observed in 9 subjects (15.0%); for 4 of these 9 subjects (44.4%) the occlusion event was acute (occurred within 0-42 days of the index procedure). A total of 6 endoAVFs (6/60 = 10%) were abandoned due to thrombosis or occlusion of the endoAVF at 12 months. The endoAVF procedure requires adjunctive procedures at the time of the index procedure, as 56/60 subjects (93.3%) in the NEAT study required the implantation of an average of 1.6 embolization coils in a brachial vein to redirect blood flow to the superficial veins and support maturation of the target cannulation area.

The probable benefits of the device are also based on nonclinical laboratory and/or animal studies as well as data collected in clinical studies as described above. In the NEAT Study, there was a high rate of procedural success as 59/60 subjects (98.3%) had an endoAVF successfully created. The 90-day maturation success rate, defined as the rate of subjects with an endoAVF that was free of stenosis or thrombosis with brachial artery flow of at least 500 mL/min and at least 4mm vein diameter OR subject was dialyzed using 2 needles, was 52/60 (86.7%). Out of the subjects who required hemodialysis during the NEAT study, 70.6% achieved cannulation success at 6 months and 86.1% achieved cannulation success at 12 months. Among those subjects who required hemodialysis during the study, functional cannulation success was

achieved in 50.4% of the subjects at 6 months and in 74.2% of the subjects at 12 months. Primary patency was achieved in 81.1% of subjects at 6 months and 73.4% of subjects at 12 months.

Additional factors to be considered in determining probable risks and benefits for the everlinQ® endoAVF System include: Physician training may reduce the rate of access site complications, and a physician training program will be used in the post-market study. The Global Analysis data and initial physician training data suggest that hemostasis of the brachial artery access site can be achieved with manual compression instead of vascular closure devices. The device requires embolization coils to be implanted in the deep veins at the time of the index procedure to assist fistula maturation, so any adjunctive procedures should be planned for each patient prior to the procedure. The device was not studied with any Black subjects, but this subgroup will be evaluated in a U.S. post-market study. All serious device- and/or procedure-related complications observed in the NEAT Study were reversible through intervention or were self-resolving. There were no device- or procedure-related infections observed in the NEAT Study.

Patient Perspectives

This submission included patient perspective information from a subset of patients treated in the NEAT Study. However, due to the limitations of the data, it was not considered in the benefit/risk analysis of the device.

Benefit/Risk Conclusion

In conclusion, given the available information above, the data support that for the creation of an arteriovenous fistula in patients with chronic kidney disease who need hemodialysis, the probable benefits outweigh the probable risks for the everlinQ® endoAVF System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the everlinQ® endoAVF System is granted and the device is classified under the following:

Product Code: PQK
Device Type: Percutaneous catheter for creation of an arteriovenous fistula for hemodialysis access
Class: II
Regulation: 21 CFR 870.1252