SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Endovascular Graft
Device Trade Name:	WRAPSODY® Cell-Impermeable Endoprosthesis
Device Procode:	PFV
Applicant's Name and Address:	Merit Medical Systems, Inc. 1600 West Merit Parkway South Jordan, Utah 84095
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P240023
Date of FDA Notice of Approval:	December 19, 2024
Breakthrough Device:	Granted breakthrough device status on March 20, 2020 (arteriovenous fistula indication) and February 26, 2021 (arteriovenous graft indication) because of reasonable expectation that the device can provide more effective treatment of a life threatening disease and availability of the device is in the best interest of the patients.

II. INDICATIONS FOR USE

The WRAPSODY® Cell-Impermeable Endoprosthesis is a flexible, self-expanding endoprosthesis indicated for use in hemodialysis patients for the treatment of stenosis or occlusion within the dialysis access outflow circuit, including stenosis or occlusion:

- in the peripheral veins of individuals with an arteriovenous (AV) fistula,
- at the venous anastomosis of a synthetic AV graft.

III. CONTRAINDICATIONS

The WRAPSODY® Cell-Impermeable Endoprosthesis (WRAPSODY CIE) has the following contraindication:

- Do not use in patients who have a known hypersensitivity to nickel or titanium.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the WRAPSODY® Cell-Impermeable Endoprosthesis labeling.

V. DEVICE DESCRIPTION

The Merit WRAPSODY® Cell-Impermeable Endoprosthesis is comprised of the WRAPSODY Endoprosthesis and the WRAPSODY delivery catheter system.

The WRAPSODY Endoprosthesis (Figure 1) is a flexible, self-expanding endoprosthesis designed for placement in the vasculature and is available in a diameter range of 6 to 16 mm and a length range of 30 to 125 mm (Table 1). The endoprosthesis is made of nitinol that is encapsulated between layers of fluoropolymer, including an expanded fluoropolymer abluminal layer, cell impermeable mid layer, and rotationally spun luminal layer. Placement of the endoprosthesis is facilitated by radiopaque markers, three on each end, that are located on both end rows of the endoprosthesis. Both ends of the endoprosthesis are trimmed in a scalloped manner.

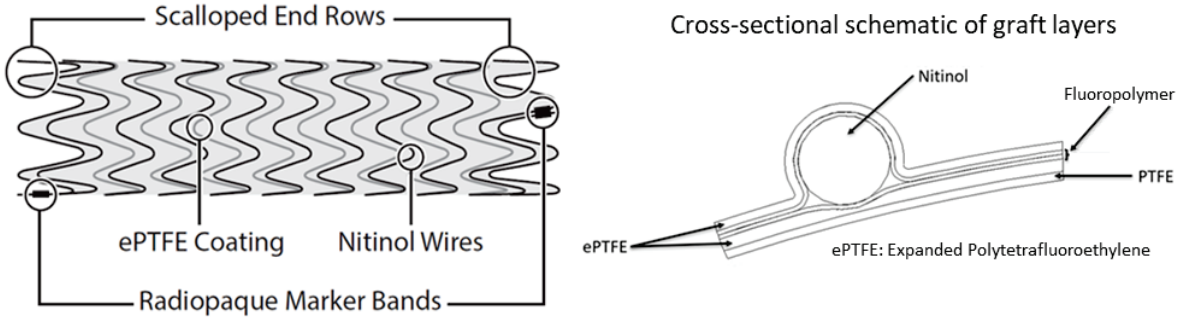


Figure 1. WRAPSODY CIE Schematic

Table 1. WRAPSODY CIE Size Range

Delivery Catheter Length (cm)	Delivery Catheter Outer Diameter (Fr)	WRAPSODY CIE Diameter (mm)	WRAPSODY CIE Length (mm)								
			30	40	50	60	70	75	80	100	125
80, 120	8	6	Not offered		X	Not offered		X	Not offered	X	X
80, 120	9	7			X			X		X	X
80, 120	9, 10	8			X			X		X	X
80, 120	10, 11	9			X			X		X	X
120	11, 12	10			X			X		X	X
120	12	12	X	X	X	X	X	Not offered	X	Not offered	
120	12, 14	14	X	X	X	X	X		X		
120	14	16	X	X	X	X	X		X		

The WRAPSODY CIE is compressed and preloaded onto the WRAPSODY delivery catheter system (Figure 2) and is housed in the endoprosthesis pod portion of the delivery catheter. The WRAPSODY delivery catheter system is designed for single-handed deployment and consists of a deployment handle that allows for controlled delivery of the WRAPSODY CIE. The working length of the WRAPSODY delivery catheter system has a hydrophilic coating and has one port with a female Luer connection for flushing both the guide wire lumen and the endoprosthesis pod. The delivery catheter shaft has radiopaque marker bands, corresponding to the proximal and distal ends of the endoprosthesis pod, to provide guidance during placement of the endoprosthesis.

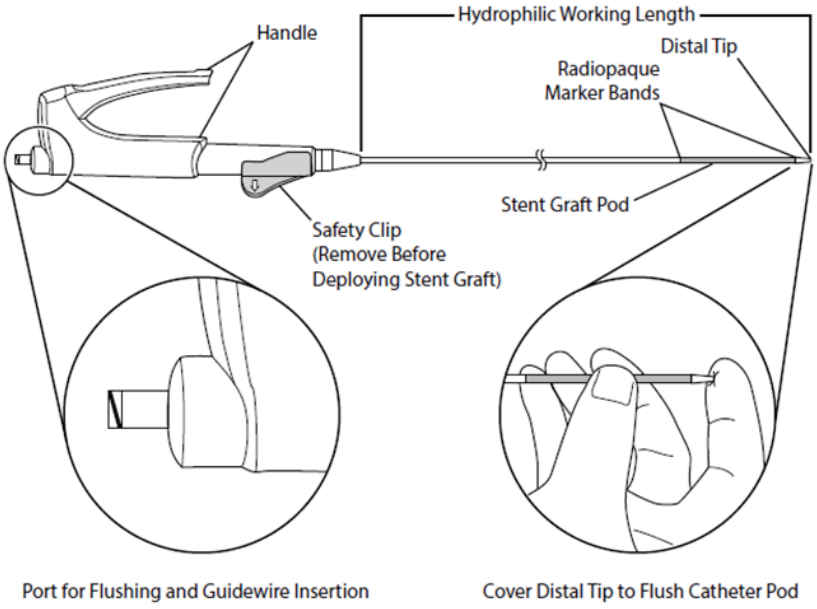


Figure 2. Wrapsody Delivery System Schematic

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are alternatives for the correction of stenosis or occlusion in the peripheral veins of hemodialysis patients with an AV fistula or at the venous anastomosis of a synthetic AV graft. Other available endovascular interventions include percutaneous angioplasty with traditional or drug coated balloons, or stenting with commercially available bare metal stents or covered stent grafts. Creation of new fistulas/grafts, different methods for dialysis (peritoneal, catheter placement), and surgical revisions may also be considered. All alternatives have advantages and disadvantages. A patient should discuss potential alternatives with their physician to select the method that may be most appropriate.

VII. MARKETING HISTORY

The WRAPSODY® Cell-Impermeable Endoprosthesis has been commercially available outside the United States since May 2020 for use in hemodialysis patients for the

treatment of stenosis or occlusion within the dialysis outflow circuit of an arteriovenous (AV) fistula or AV graft. The product has been commercialized in the European Union, Andorra, Argentina, Australia, Brazil, Canada, Chile, Colombia, Ecuador, Egypt, Hong Kong, Israel, Mexico, New Zealand, Norway, Panama, Peru, Saudi Arabia, South Africa, Switzerland, United Arab Emirates, and the United Kingdom.

The device has never been withdrawn from any market for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) that may be associated with the use of the WRAPSODY CIE and delivery catheter system, including those that have been reported in association with conventional vascular stents and endoprostheses.

Potential endoprosthesis-related adverse effects:

- Aneurysm
- Embolism and/or vessel thrombosis
- Emergency or non-emergency access circuit intervention
- Endoprosthesis compression
- Endoprosthesis embolization
- Endoprosthesis kinking
- Endoprosthesis malfunction
- Endoprosthesis migration
- Endoprosthesis misplacement
- Endoprosthesis occlusion / thrombosis
- Fracture of the endoprosthesis that may or may not lead to embolism, serious injury or surgical intervention
- Infection or fever, including device infection
- Insufficient endoprosthesis expansion
- Ischemia
- New lesion or total occlusion of the vascular access circuit
- Placement of a bailout stent / stent graft
- Pseudoaneurysm
- Restenosis of the treated segment
- Serious injury requiring surgical intervention
- Steal syndrome
- Vascular complications that may require surgical repair (conversion to open surgery)

Potential delivery catheter system-related adverse effects:

- Access-site complications
- Bond joint failure
- Delivery system kinking
- Delivery system malfunction that may or may not lead to device embolism,

serious injury, or surgical intervention
- Detachment of part
- Failure to deploy
- Fracture of the guide wire or any component of the delivery catheter system that may or may not lead to embolism, serious injury or surgical intervention
- Hematoma
- High deployment forces
- Inability to track to the target location
- Inaccurate deployment
- Incompatibility with accessory devices
- Premature deployment
- Seroma

Potential procedure-related adverse effects:
- Access-site complications
- Allergic reaction to contrast media / medications
- Arteriovenous (AV) fistula
- Bleeding complications
- Cardiac arrest
- Cardiac arrhythmia
- Death
- Extravasation of contrast media
- Hematoma
- Infection or fever
- Ischemia
- Myocardial infarction or coronary ischemia
- Neurological deficit
- Pain
- Radiation exposure
- Reaction to contrast media / medication
- Respiratory distress or failure
- Serious injury requiring surgical intervention
- Seroma
- Stroke or TIA
- Swelling or edema
- Transfusion
- Vascular complications that may require surgical repair (conversion to open surgery)
- Vessel dissection
- Vessel perforation
- Vessel rupture
- Vessel spasm

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

IX. SUMMARY OF NONCLINICAL STUDIES

A comprehensive set of nonclinical bench, biocompatibility, packaging, and sterilization testing was performed to support the safety and effectiveness of the WRAPSODY® Cell-Impermeable Endoprosthesis for the proposed intended use.

A. Biocompatibility

Biocompatibility testing was performed in accordance with applicable sections of ISO 10993, *Biological evaluation of medical devices – Part 1: Evaluation and testing* and the FDA guidance documents *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"* and *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems*. Testing was conducted on final, sterilized devices manufactured in accordance with standard operating procedures and representative of finished product. Components of the WRAPSODY CIE and delivery catheter system were categorized per ISO 10993-1 based on the intended duration and contact with or within the body and specific biocompatibility tests were performed based on this categorization. The WRAPSODY CIE was categorized as an implant device with permanent exposure to circulating blood (>30 days), and the delivery catheter system was categorized as an externally communicating device with limited (≤24 hours) contact with circulating blood.

Table 2 and Table 3 summarize the biocompatibility test results for both the WRAPSODY CIE and delivery catheter system, respectively. Biocompatibility testing was performed in accordance with Good Laboratory Practice (GLP) regulations (21 CFR Part 58).

Table 2. Summary Results of Biocompatibility Testing for WRAPSODY CIE

Test Name	Test Description	Results
Cytotoxicity	L929 MEM Elution	Non-toxic
Sensitization	Guinea Pig Maximization Sensitization	Non-sensitizing
Irritation	Intracutaneous Injection	Non-irritating
Acute Systemic Toxicity	Systemic Injection	Non-toxic
Material Mediated Pyrogenicity	Rabbit Pyrogenicity	Non-pyrogenic
Subacute/Subchronic Toxicity	In Vivo Toxicity Study	Non-toxic
Genotoxicity	Bacterial Reverse Mutation	Non-mutagenic
	Mouse Lymphoma Assay	
Implantation	In Vivo Implantation Studies*	Non-toxic
Hemocompatibility – Hemolysis	Direct and Indirect Contact	Non-hemolytic
Hemocompatibility – Complement Activation	Direct Contact	Not a complement activator
Hemocompatibility – Thrombogenicity	In Vivo Implantation Studies*	Non-thrombogenic
Chronic Toxicity	In Vivo Toxicity Study*	Non-toxic

* Evaluated as part of the animal studies outlined in Section D.

Chemical characterization and associated toxicological risk assessments were performed. These studies supported the acceptable biological risk for the WRAPSODY CIE, including for the endpoint of carcinogenicity.

Table 3. Summary Results of Biocompatibility Testing for WRAPSODY Delivery Catheter System

Test Name	Test Description	Results
Cytotoxicity	L929 MEM Elution	Non-toxic
Sensitization	Guinea Pig Maximization Sensitization	Non-sensitizing
Irritation	Intracutaneous Injection	Non-irritating
Acute Systemic Toxicity	Systemic Injection	Non-toxic
Material Mediated Pyrogenicity	Rabbit Pyrogenicity	Non-pyrogenic
Hemocompatibility – Hemolysis	Direct and Indirect Contact	Non-hemolytic
Hemocompatibility – Complement Activation	Direct Contact	Not a complement activator
Hemocompatibility – Thrombogenicity	In Vivo Thrombogenicity	Non-thrombogenic

B. Laboratory Studies

In vitro bench testing was conducted as part of design verification and validation to support the safety and effectiveness of the WRAPSODY® Cell-Impermeable Endoprosthesis. This testing was conducted based on recommendations from risk assessments with consideration of FDA guidances and industry-recognized standards, including FDA's Guidance for Industry and FDA Staff: *Non-Clinical Engineering Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems,* ISO 25539-1:2017 *Cardiovascular implants – Endovascular devices – Part 1: Endovascular prostheses*, and ISO 10555-1:2013/Amd 1:2017 *Intravascular Catheters – Sterile And Single-Use Catheters – Part 1: General requirements*. The bench test results are summarized in Table 4. The testing presented in Table 4 includes results from both baseline and aged devices where appropriate.

Table 4. Summary Results of Non-Clinical Laboratory Studies

Test	Purpose	Acceptance Criteria	Results
WRAPSODY CIE			
Material Composition	Verify the chemical composition of the endoprosthesis	Characterization only	Chemical composition of the endoprosthesis was characterized
Shape Memory and Superelasticity of Intravascular Stents	Verify the transition temperature of the nitinol implant	A_f temperature ≤ 37.0 ºC	Pass

Test	Purpose	Acceptance Criteria	Results
Stent Corrosion Resistance	Verify the implant's ability to resist corrosion	Pitting Corrosion Breakdown potential (Eb) > 600 mV for all test articles; Galvanic Corrosion Performed for characterization only	Pass
Nickel Ion Release Testing	Verify the potential for nickel ion release	Maximum nickel release rate must be < 35 µg/day for all specimens throughout the testing duration	Pass
Dimensional Verification*	Verify that critical implant dimensions are met	Labeled length ±1 mm Labeled inside diameter ±0.4 mm	Pass
Foreshortening*	Evaluate the relationship between implant length and diameter following deployment	Characterization only	Foreshortening response characterized for inclusion in labeling
Endoprosthesis Integrity*	Evaluate graft integrity after loading and deployment	Free from mechanical defects including through holes, cracks, scratches, permanent set, and graft layer delamination; no dirt, soiled areas, spots, stains, embedded particles, or other defects that would render the device unsuitable for its intended use	Pass
Radial Outward Force*	Evaluate the radial outward force exerted by the endoprosthesis as a function of diameter	≥ 0.078 N/mm and ≤ 0.709 N/mm	Pass
Mechanical Properties*	Evaluate the longitudinal tensile strength of the endoprosthesis	≥ 15 N	Pass
Stress / Strain Analysis	Evaluate mechanical and physical response and performance characteristics of the endoprosthesis	Safety factor > 1.0	Pass
Fatigue Analysis	Evaluate the nitinol strain-life fatigue durability performance		
10-year Accelerated Durability Testing – Multi-Axis Loading	Evaluate the durability and fatigue life of the endoprosthesis under multi axis loading (axial, longitudinal, rotational)	No fractures, detachment or delamination of the stent from the covering, tearing or holes in the endoprosthesis covering, failure of the stent crimps, or permanent deformation of the stent lumen	Pass
10-year Accelerated Durability Testing – Pulsatile Loading	Evaluate the durability and fatigue life of the endoprosthesis under pulsatile loading		Pass

Test	Purpose	Acceptance Criteria	Results
Particulate Evaluation*	Evaluate the particulate generated from endoprosthesis deployment	Characterization only	Characterized and determined to be acceptable
Magnetic Resonance Imaging (MRI) Safety and Compatibility	Evaluate MRI safety and compatibility	Characterization only	MR Conditional at field strength of 1.5 T and 3.0 T
Radiopacity	Evaluate radiopacity of the endoprosthesis	Visibility of the implant under fluoroscopy must be rated as clinically acceptable by physician experts in an animal model	Pass
Compression Resistance*	Evaluate the compression resistance of the endoprosthesis	Compression resistance ≥ 0.076 N/mm length	Pass
Kink Resistance*	Evaluate the minimum radius that the endoprosthesis can accommodate without kinking	Maximum kink radius of 13.95 mm for 6, 7, 8, 9, and 10 mm diameters; maximum kink radius of 28.60 mm for 12, 14, and 16 mm diameters	Pass
Porosity*	Evaluate the pore area and fiber thickness of the luminal surface	Endoprosthesis must meet the porosity criteria specified as acceptable for the intended use	Pass
Migration Resistance*	Evaluate the migration resistance of the endoprosthesis	Characterization only	Characterized and determined to be acceptable
Strength of Stent/Attachment System to Graft Bond*	Evaluate the strength of the bond between graft materials and the stent frame	Characterization only	Characterized and determined to be acceptable
Burst Strength*	Evaluate the burst / circumferential strength of the endoprosthesis	≥ 33.0 PSI	Pass
Integral Water Permeability (IWP) and Water Entry Pressure (WEP)*	Evaluate the IWP and WEP attributes of the endoprosthesis	Endoprosthesis must meet the IWP criteria specified as acceptable for the intended use WEP evaluated for characterization only	Pass
WRAPSODY DELIVERY CATHETER SYSTEM			
Dimensional Verification*	Evaluate the delivery system dimensions and dimensional compatibility with accessory devices	Actual length ≥ labeled working length Guide wire lumen internal diameter: 0.037" ± 0.001" Maximum catheter working length outer diameter: labeled French size plus 0.4 French	Pass

Test	Purpose	Acceptance Criteria	Results
Simulated Use – Delivery, Deployment, and Retraction*	Evaluate performance of the device under simulated use conditions	Delivery system must meet pre-deployment and post-deployment visual checks (i.e., free from damage and unacceptable catheter gaps) Endovascular System must meet the following: -Ability to flush catheter guidewire lumen and endoprosthesis pod -Ability to advance to desired deployment location and deploy stent without mechanical failure of delivery system -Deployment Accuracy: ± 7 mm from target deployment location. -Endoprosthesis is fully apposed to vessel wall following deployment. -Delivery system may be removed from vessel as a complete unit without separation or damage to accessory devices. -Endoprosthesis is compatible with PTA balloons -Visual particulate is not observed -Compatibility with accessory components -Lumen of deployed endoprosthesis is open and not obstructed post deployment -Post Deployment, endoprosthesis meets integrity criteria -Endoprosthesis remains stationary under simulated use -Deployment of overlapping devices is achieved	Pass
Catheter Bond Strength and Tip Pull Test*	Evaluate the longitudinal bond strength between parts of the delivery system	Catheter to catheter: ≥ 24.2 lbf Carrier mechanism to catheter: ≥ 24.2 lbf Guide wire lumen to Luer, flush hole, and tip: ≥ 3.0 lbf Cannula/hypotube to Luer: characterization only Handle mechanism strength: ≥ 24.2 lbf	Pass
Flexibility and Kink Test*	Evaluate the minimum radius the delivery system can accommodate without kinking	No kink at a radius ≥ 50.8 mm	Pass
Torque Strength*	Evaluate the torque required to cause failure of the joints and/or fixed connections of the delivery system	Characterization only	Characterized and determined to be acceptable
Force to Deploy*	Evaluate the force required to deploy the endoprosthesis from the delivery system	< 24.2 lbf	Pass

Test	Purpose	Acceptance Criteria	Results
Luer Fitting and Hemostasis Evaluation*	Confirm Luer fitting conforms to recognized standards and ensure ability of delivery system to maintain adequate hemostatic seal during use	Meet applicable requirements of ISO 594-1, ISO 594-2, and ISO 80369-7	Pass
Lubricity*	Evaluate lubricity of the delivery system	Peak friction force ≤ 52.5 gf	Pass

* Testing also conducted at real-time and accelerated aged time points

C. Sterility, Packaging and Shelf-Life Testing

The WRAPSODY® Cell-Impermeable Endoprosthesis is sterilized by Ethylene Oxide (EO) to provide a Sterility Assurance Level (SAL) of 10^{-6}. The EO sterilization cycles were validated in accordance with AAMI/ANSI/ISO 11135, *Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices.*

Packaging validation conducted for the WRAPSODY® Cell-Impermeable Endoprosthesis demonstrates the ability of the packaging to protect the product and to maintain a sterile barrier through shipping and shelf life. Evaluations were conducted in accordance with EN ISO 11607-1:2020, *Packaging for terminally sterilized medical devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems* and EN ISO 11607-2:2020, *Packaging for terminally sterilized medical devices – Part 2: Validation requirements for forming, sealing and assembly processes.*

Table 5. Summary Results of Packaging Studies

Test	Purpose	Acceptance Criteria	Results
WRAPSODY Packaging			
Visual Inspection*	Evaluate damage and defects to the package and labeling	Defects should not be apparent to the pouches, labels, patient ID cards, cartons, and shippers.	Pass
Dye Penetration*	Evaluate integrity of sterile barrier	No dye leaks through seals of the pouches within 5 seconds of dye contacting the seal. Half of the seal remaining due to seal creep	Pass
Bubble Emission*		No steady stream of bubbles from the pouches	Pass
Peel Test*	Evaluate strength of sterile barrier seals	No peel test values less than 1 lb/in.	Pass
Engineering Evaluation	Evaluate damage to the device	Air flow was assessed and the device was visually inspected for damage	Pass
Aseptic Presentation	Evaluate package usability	Ease to open the package, removal of package contents, and size of packaging for hospital use must be clinically acceptable (rank ≥ 3)	Pass
Burst Testing+	Evaluate integrity of sterile barrier	≥ 8 in H_2O	Pass

* Testing also conducted at real-time and accelerated aged time points
+ Testing only conducted at real-time and accelerated aged time points

A shelf life of 3.5 years was established for the WRAPSODY® Cell-Impermeable Endoprosthesis based on product and package shelf life testing. The specific engineering tests completed to support the shelf life are denoted by an asterisk (*) in Table 4 and Table 5.

D. Animal Studies

Three primary large-animal studies have been completed for the WRAPSODY® Cell-Impermeable Endoprosthesis, including two chronic GLP studies to assess safety and performance, and one acute non-GLP study to evaluate device performance and handling. Results of these animal studies are summarized in Table 6. GLP studies were conducted in accordance with 21 CFR Part 58.

Table 6. Summary Results of Primary Animal Studies

Study	Purpose	# of Animals	Endpoints	Endpoints Met
GLP Ovine AV Fistula Model (35 days)	Assess the thrombus, patency, and cell and tissue response to implant through gross necropsy and histology; assess acceptability of delivery catheter	8 animals were implanted with contralateral test (n=11 WRAPSODY CIE) and control (n=9 Fluency™) devices and followed for 7 or 35 days	Adverse health related issues; Migration; Quantitative angiography; Catheter performance and interaction with accessory devices; Pathology of non-target organs; Thrombogenicity; Histology (morphometry); Vessel injury; Biological response of vessel	Yes
GLP Healthy Ovine Arterial Model (180 days)	Assess the thrombus, patency, and cell and tissue response to implant through gross necropsy, histology, and immunochemistry; assess acceptability of delivery catheter	17 animals were implanted with contralateral test (n=22 WRAPSODY CIE) and control (n=21 Fluency™) devices and followed for 30, 90, or 180 days	Adverse health related issues; Migration; Quantitative angiography; Catheter performance and interaction with accessory devices; Pathology of non-target organs; Thrombogenicity; Histology (morphometry); Vessel injury; Biological response of vessel; Pathology of peripheral tissues	Yes
Acute Porcine Model (non-GLP)	Evaluate acute performance characteristics of the device during and immediately post-implantation	2 animals were implanted with a total of 23 test devices (WRAPSODY CIE)	Quantitative angiography; Radiopacity; Migration; Delivery and deployment; Adverse events; Packaging	Yes

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of vascular access interventions with the WRAPSODY® Cell-Impermeable Endoprosthesis for the correction of stenosis or occlusion in the peripheral veins of

hemodialysis patients with an AV fistula or at the venous anastomosis of a synthetic AV graft in the United States, United Kingdom, Canada, and Brazil under IDE # G200150. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between March 9, 2021, and August 2, 2023. The database for this PMA reflected data collected through March 19, 2024, and included 358 subjects. This includes 246 subjects in the AVF Peripheral cohort and 112 subjects in the AVG Anastomosis cohort. There were 43 investigational sites, including 33 sites in the United States, 5 sites in the United Kingdom, 1 site in Canada, and 4 sites in Brazil.

The WRAPSODY WAVE study was a prospective, multi-center, multi-cohort study consisting of a randomized concurrently-controlled AVF cohort and a single arm AVG cohort.

Subjects in the AVF cohort were prospectively randomized (1:1) to treatment with the WRAPSODY® Cell-Impermeable Endoprosthesis or PTA, a legally marketed alternative with similar indications for use. All subjects in the AVG cohort were treated with the WRAPSODY® Cell-Impermeable Endoprosthesis.

The primary safety outcome measure was the proportion of subjects without any localized or systemic safety events through 30 days post-procedure that affected the access or venous outflow circuit and resulted in reintervention, hospitalization, or death; specific events of clinically-driven target lesion revascularization (CD-TLR) or reintervention due to target lesion thrombosis were counted as failures of primary effectiveness and not included as failures of primary safety. The following hypotheses were tested for the primary safety endpoint:

- AVF cohort: The event-free rate is determined to be non-inferior in the treatment arm compared to the control arm based on the Farrington-Manning test (p-value < 0.05).
- AVG cohort: The primary safety endpoint was evaluated against a literature-based performance goal (PG) of 89% freedom from safety events. This safety PG was established based on literature for other stent grafts.[1] The safety PG is met if the binomial exact test resulted in a single-sided p-value less than 0.05.

The primary effectiveness outcome measure was Target Lesion Primary Patency (TLPP) at 6 months, defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or target lesion thrombosis measured through 6 months post-procedure, which is the time interval of uninterrupted patency after the study

[1] Inclusive of results from clinical investigations for the FLAIR® Endovascular Stent Graft, GORE® VIABAHN® Endoprosthesis with Heparin Bioactive Surface (REVISE study), FLUENCY® PLUS Endovascular Stent Graft (RESCUE study), and Bard COVERA™ Vascular Covered Stent (AVeVA study)

procedure to the next intervention performed on the target lesion or uncorrectable target lesion occlusion. The following hypotheses were tested for the primary effectiveness endpoint:

- AVF cohort: The proportion of subjects achieving TLPP at 6 months for the treatment arm is superior to that in subjects treated with PTA alone. A two-sided p-value was calculated based on the chi-square test with a significance level of 0.05.
- AVG cohort: The primary effectiveness endpoint was evaluated against a literature-based PG of 60%, which represents the average 6-month TLPP reported for other stent grafts utilized for this indication.[1] The effectiveness PG is considered met if the one-sided p-value is less than 0.05 based on the binomial exact test.

The study was overseen by an independent Data Safety Monitoring Board (DSMB) in accordance with an established DSMB charter. An independent Clinical Events Committee (CEC) adjudicated predefined clinical events reported during the study in accordance with the CEC charter. An independent core laboratory provided uniformly defined pre- and post-operative imaging analysis.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the WRAPSODY WAVE study was limited to patients who met specific inclusion criteria, including:

   General Inclusion Criteria

   1. Subject is male or female, with an age ≥ 18 years.
   2. Subject has a life expectancy ≥ 12 months.
   3. Subject is undergoing chronic hemodialysis.
   4. Subject has either a mature AVF or AVG in the arm ≥30 days prior to the index procedure and has completed at least one successful dialysis session.
   5. Subject has clinical and/or hemodynamic evidence of a venous outflow obstruction or AV fistula or graft dysfunction.

   Angiographic Inclusion Criteria

   1. Target lesion originates ≥3 cm from the cannulation segment (needling zone).
   2. Target lesion is located:
      a. In an arm (including the cephalic arch) in a subject with AVF, and not in the cannulation segment (needling zone), OR
      b. At the anastomosis or juxta-anastomosis in a subject with AVG.
   3. Target lesion involves a de novo stenotic or non-stented restenotic lesion.
   4. Target lesion is ≥5 cm from arterial anastomosis.
   5. Target lesion has ≥50% stenosis.
   6. Target lesion reference vessel diameter is between 5.0 mm and 14.0 mm.
   7. Single or multiple target lesions measuring ≤10 cm in overall length.

8. Single or multiple target lesions must be able to be covered by a single stent graft or multiple overlapping stent grafts. (Note: multiple target lesions must be treated as a single lesion with a maximum length of 10 cm.)
9. Successful predilatation of the target lesion defined as crossing of the guide wire resulting in full expansion of the predilatation balloon.
10. Subject has up to one (1) non-target outflow lesion requiring intervention at the index procedure. Non-target lesion must be at least 10 cm away from the target lesion. Non-target lesion may only be treated with standard PTA.
11. Subject has no stent graft or has a stent graft in the access circuit that is ≥30 days since placement, is patent (≤30% stenosis) and is ≥3 cm from target lesion.
12. Non-target lesion has been successfully treated at time of index procedure (success measured as ≤30% residual stenosis and without complication).

Patients were <u>not</u> permitted to enroll in the WRAPSODY WAVE study if they met specific exclusion criteria, including:

General Exclusion Criteria

1. Subject has any planned major surgical or endovascular procedures within 30 days after the index procedure.
2. Subject has a planned surgical revision of access site.
3. Subject has a known or suspected infection of the hemodialysis access site, systemic infection and/or septicemia.
4. Subject has a known active coagulopathy or bleeding diatheses.
5. Known hypersensitivity to nickel titanium alloy.
6. Subject has a stroke diagnosis within 3 months prior to enrollment.
7. Subject has a history of unstable angina or myocardial infarction within 60 days prior to enrollment.
8. Subject has a contraindication to antiplatelet, anticoagulant, or thrombolytic therapies.
9. Subject has known allergy to contrast agents or medications used to perform endovascular intervention that cannot be adequately pre-medicated.
10. Subject is pregnant, breastfeeding, or intending to become pregnant within the next year.
11. Subject has a stent or stent graft located anywhere in the AV access circuit that is not patent (>30% stenosis) or implanted <30 days.
12. Fistula was created via an endovascular procedure.
13. Current permanent central venous catheter for dialysis access.
14. Subject's hemodialysis access is anticipated to be abandoned within 6 months.
15. Subject is scheduled for kidney transplant or peritoneal dialysis within the next 6 months post-procedure.
16. Planned concomitant procedure during the index procedure.

17. Active malignancy other than non-melanomatous skin cancer.
18. Subject is participating in another research study involving an investigational product.
19. Subject has other medical, social or psychological problems that, in the opinion of the investigator, preclude them from receiving this treatment, and the procedures and evaluations pre- and post-treatment.
20. Subject has a non-synthetic graft requiring treatment as the target lesion.

Angiographic Exclusion Criteria

1. Target lesion is located within a stent / stent graft.
2. Target lesion treatment would involve the cannulation segment.
3. Target lesion is <5cm from arterial anastomosis.
4. Evidence of aneurysm, pseudoaneurysm or acute thrombus within the target lesion.
5. Target lesion is, and/or WRAPSODY CIE would be placed in any part of: in the superior vena cava, in the jugular vein, under the clavicle, across the elbow, in the cannulation segment, within any part of a pre-existing stent or stent graft (other than an access arteriovenous graft), lower extremity, non-synthetic graft, any vessels central to the cephalic arch vein.
6. Lesion is located such that placement of a WRAPSODY CIE would result in a 'hinge' area requiring bridge stenting between the endoprosthesis and an existing stent or stent graft.
7. More than two (2) lesions in the venous outflow circuit with ≥50% stenosis requiring intervention. Non-target lesion has not been successfully treated at time of index procedure.
8. Subject has more than one (1) non-target lesion (≥50% stenosis) requiring intervention at the index procedure.
9. There is lack of full expansion of the predilatation balloon.
10. Target lesion(s) requires percutaneous interventional treatment, beyond standard balloon angioplasty alone, prior to randomization and/or investigational device use.

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examinations at 30 days and 3, 6, 9 12, 18, and 24 months. Table 7 provides the parameters assessed during the preoperative baseline assessment and the data collection schedule through the 24-month visit. Adverse events and complications were recorded at all visits. The key timepoints are shown below in the tables summarizing safety and effectiveness.

Table 7. Follow-up Schedule

Visit Schedule	Baseline	Day 0 (Index Procedure)	30 Days (± 10 days)	3 Months (90 ± 15 days)	6 Months (180 ± 30 days)	9 Months (270 ± 30 days)	12 Months (360 ± 45 days)	18 Months (545 ± 45 days)	24 Months (720 ± 75 days)
Informed Consent	X								
Inclusion / Exclusion Criteria Evaluation	X	X							
Demographics	X								
Medical History	X								
Physical Examination, including physical assessment of fistula or graft / access circuit	X		X		X		X		X
Dialysis Status	X		X		X		X		X
Anti-coagulation / Anti-platelet Medications	X	X	X	X	X	X	X	X	X
Index Angiography		X							
Adverse Event		X	X	X	X	X	X	X	X

3. Clinical Endpoints

With regards to safety, the proportion of subjects without any localized or systemic safety events through 30 days post-procedure that affected the access or venous outflow circuit and resulted in reintervention, hospitalization, or death was evaluated; specific events of CD-TLR or reintervention due to target lesion thrombosis were counted as failures of primary effectiveness and not included as failures of primary safety.

With regards to effectiveness, Target Lesion Primary Patency (TLPP) at 6 months was evaluated. TLPP was defined as freedom from clinically-driven target lesion revascularization (CD-TLR) or target lesion thrombosis measured through 6 months post-procedure, which is the time interval of uninterrupted patency after the study procedure to the next intervention performed on the target lesion or uncorrectable target lesion occlusion.

Secondary effectiveness endpoints with hypothesis testing included:

- TLPP at 12 and 24 months
- Access Circuit Primary Patency (ACPP) at 6, 12, and 24 months, defined as time to loss of Primary Patency of the access circuit, which is the time from post-procedure until any venous outflow circuit re-intervention, or access thrombosis or abandonment.

Other important secondary endpoints that are summarized with descriptive

statistics included:

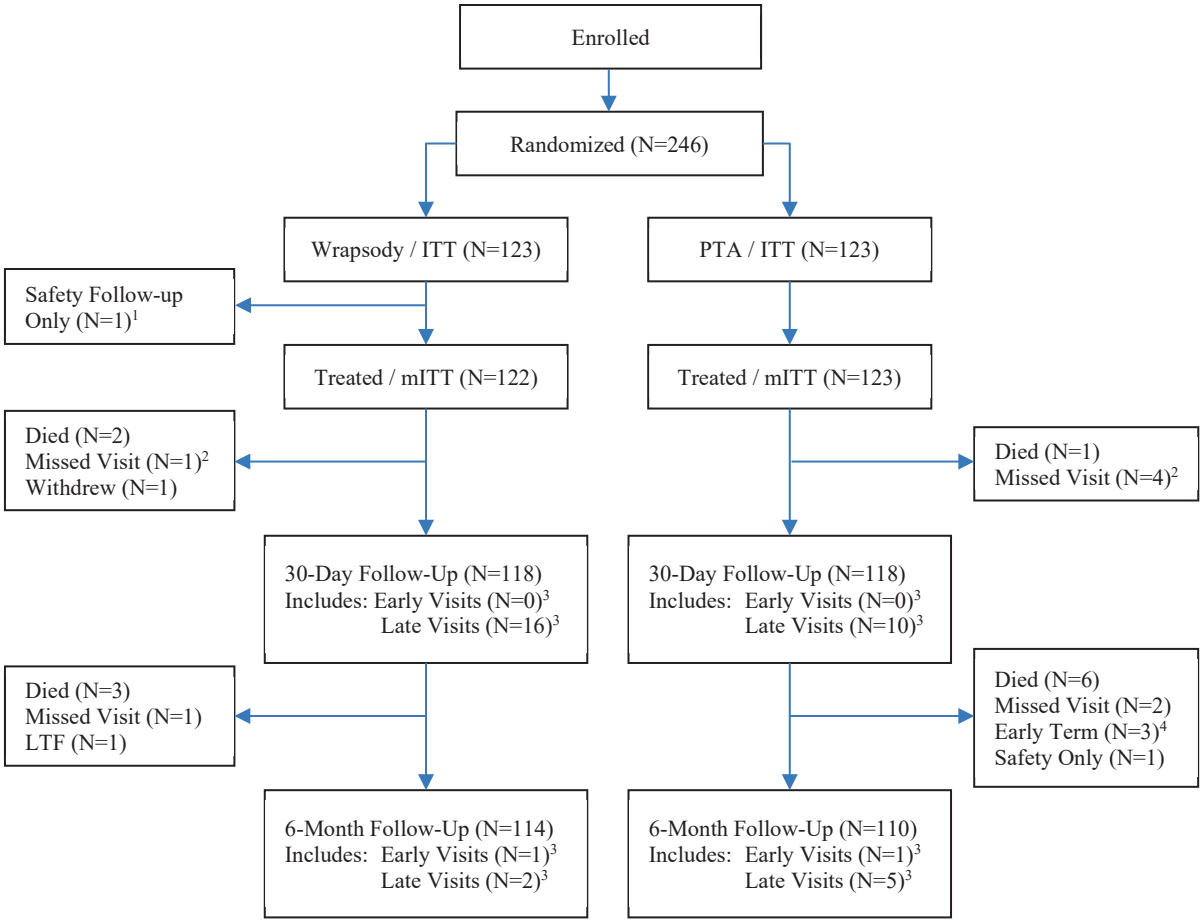
- Post-Procedure Secondary Patency defined as the interval post-procedure until access circuit abandonment.
- Rate of device observations and potential malfunctions or failures.
- Rate of Serious Adverse Events (SAE).
- Rate of SAE involving the AV access circuit.
- Number of target lesion reinterventions to maintain target lesion patency.
- Number of interventions to maintain access circuit patency.
- Percentage of subjects with Device and Procedure Success.
    - Device Success: Successful delivery to the target lesion, deployment and retrieval of delivery system at index procedure.
    - Procedure Success: At least one indicator of hemodynamic success (e.g., physical examination with restoration of a thrill, direct measurement of flow) in the absence of peri-procedural (index procedure through discharge) Serious Adverse Device Effects.

Exploratory endpoints:

- Clinical Success defined as resumption of successful dialysis through existing access for at least one session following initial study procedure.
- Index of Patency Function at months 6, 12 and 24 defined as time after study procedure to complete access abandonment divided by number of venous outflow circuit re-interventions to maintain hemodialysis.

B. Accountability of PMA Cohort

Overall, 358 subjects were enrolled in the WRAPSODY WAVE study. A total of 246 subjects were enrolled in the AVF cohort and 112 subjects were enrolled in the AVG cohort. The number of subjects available for analysis at each time point is shown in Figure 3 for the AVF cohort and Figure 4 for the AVG cohort. The Intent to Treat (ITT) population includes all randomized subjects in the AVF cohort, and all subjects enrolled in the AVG cohort. The Modified Intent to Treat (mITT) population includes all ITT subjects who received treatment.



[1] One patient was not treated with the WRAPSODY CIE due to procedural complication of extravasation after pre-dilation and randomization that required treatment on an emergent basis with a commercial stent
[2] Subjects with missed visits at 30 days are not exited from study and remain eligible for 6-month follow-up.
[3] Early and Late Visits occurred outside of the protocol-defined follow-up windows (i.e., 30 ± 10 days, 180 ± 30 days)
[4] Reasons for early termination (early term) include, but are not limited to, subjects who proceed to kidney transplant and access circuit abandonment

Figure 3. Patient Accountability for AVF Cohort

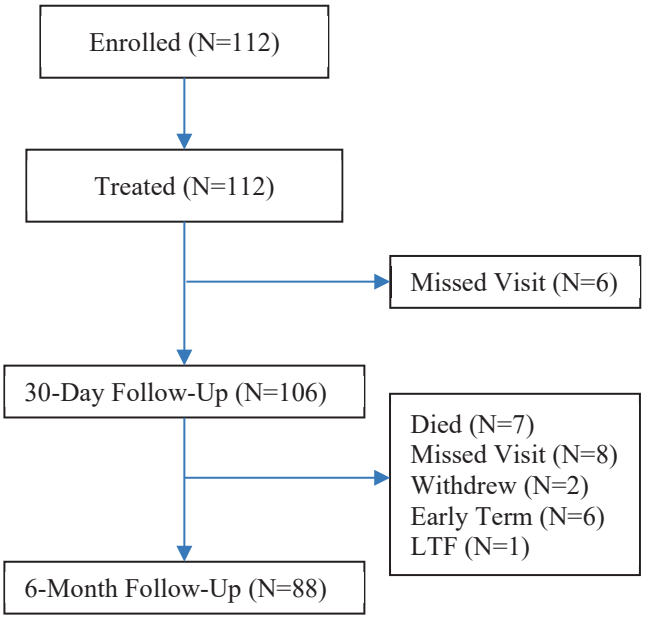


Figure 4. Patient Accountability for AVG Cohort

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a vascular access intervention study performed in the US. Demographics and Medical history are reported in Table 8 and Table 9.

In the AVF and AVG cohorts respectively, 43% and 54% of subjects were female, 52% and 30% were Caucasian / white, 41% and 62% were African American / black, and 32% and 25% reported Hispanic / Latino ethnicity. The rate of unstable angina was higher in the PTA group compared to the WRAPSODY group, while the rates of congestive heart failure and peripheral vascular disease were higher in the WRAPSODY group compared to the PTA group.

Baseline characteristics of the access circuit and target lesion are provided in Table 10 and Table 11. Based on core laboratory measurements, the length of the stenosis being treated was longer in the WRAPSODY group compared to the PTA group. Overall, 60% of AVF lesions and 53% of AVG lesions enrolled in the study were being treated for restenosis.

The number of subjects implanted with each size of WRAPSODY CIE is provided in Table 12.

Table 8. Demographics

Parameter	AVF Cohort		AVG Cohort
	WRAPSODY (n=122)	PTA (n=123)	WRAPSODY (n=112)
Age at enrollment (years)	61.6 ± 13.9	60.1 ± 14.5	64.1 ± 13.3
BMI*	29.6 ± 6.5	29.5 ± 7.5	27.0 ± 6.3
Sex			
Male	70 / 122 (57.4%)	69 / 123 (56.1%)	51 / 112 (45.5%)
Female	52 / 122 (42.6%)	54 / 123 (43.9%)	61 / 112 (54.5%)
Race			
Caucasian / White	66 / 122 (54.1%)	62 / 123 (50.4%)	34 / 112 (30.4%)
African American / Black	49 / 122 (40.2%)	51 / 123 (41.5%)	69 / 112 (61.6%)
American Indian or Alaska Native	2 / 122 (1.6%)	0 / 123 (0.0%)	1 / 112 (0.9%)
Pacific Islander	1 / 122 (0.8%)	0 / 123 (0.0%)	0 / 112 (0.0%)
Asian	3 / 122 (2.5%)	6 / 123 (4.9%)	3 / 112 (2.7%)
Other	3 / 122 (2.5%)	4 / 123 (3.3%)	5 / 112 (4.5%)
Ethnicity			
Non-Hispanic / Latino	81 / 122 (66.4%)	86 / 123 (69.9%)	83 / 111 (74.8%)
Hispanic / Non-Latino	41 / 122 (33.6%)	37 / 123 (30.1%)	28 / 111 (25.2%)

Table 9. Medical History

Parameter	AVF Cohort		AVG Cohort
	WRAPSODY (n=122)	PTA (n=123)	WRAPSODY (n=112)
Cerebrovascular Accident (CVA) or Stroke	18 / 122 (14.8%)	16 / 123 (13.0%)	18 / 111 (16.2%)
Transient Ischemic Attack (TIA)	11 / 122 (9.0%)	10 / 121 (8.3%)	8 / 109 (7.3%)
Cardiac Arrythmia	30 / 121 (24.8%)	18 / 120 (15.0%)	19 / 109 (17.4%)
Hypertension	115 / 122 (94.3%)	116 / 123 (94.3%)	106 / 112 (94.6%)
History of / or current hypercholesterolemia / dyslipidemia	71 / 121 (58.7%)	74 / 119 (62.2%)	62 / 109 (56.9%)
Premature atherosclerotic disease	18 / 119 (15.1%)	21 / 121 (17.4%)	17 / 110 (15.5%)
Unstable angina	1 / 121 (0.8%)	7 / 120 (5.8%)	1 / 112 (0.9%)
Previous MI	18 / 121 (14.9%)	21 / 123 (17.1%)	22 / 111 (19.8%)
Previous PCI	13 / 119 (10.9%)	20 / 118 (16.9%)	15 / 109 (13.8%)
Previous CABG	10 / 122 (8.2%)	13 / 121 (10.7%)	15 / 112 (13.4%)
Congestive Heart Failure (CHF)	42 / 121 (34.7%)	27 / 122 (22.1%)	35 / 110 (31.8%)
Peripheral Vascular Disease (PVD)	20 / 122 (16.4%)	8 / 118 (6.8%)	21 / 109 (19.3%)
Smoking	51 / 120 (42.5%)	50 / 122 (41.0%)	52 / 110 (47.3%)
Current	8 / 51 (15.7%)	12 / 50 (24.0%)	13 / 52 (25.0%)
Diabetes Mellitus	88 / 122 (72.1%)	79 / 122 (64.8%)	70 / 112 (62.5%)
Type I	4 / 88 (4.5%)	11 / 79 (13.9%)	11 / 70 (15.7%)
Type II	82 / 88 (93.2%)	67 / 79 (84.8%)	57 / 70 (81.4%)
Unknown	2 / 88 (2.3%)	1 / 79 (1.3%)	2 / 70 (2.9%)
Gastro-Intestinal (GI) / Genito-Urinary (GU) bleeding	11 / 122 (9.0%)	5 / 120 (4.2%)	13 / 109 (11.9%)
Substance abuse	9 / 119 (7.6%)	7 / 119 (5.9%)	14 / 110 (12.7%)
Other significant medical history	66 / 122 (54.1%)	52 / 122 (42.6%)	60 / 112 (53.6%)

Table 10. Access Circuit Assessment at Baseline

Parameter	AVF Cohort		AVG Cohort
	WRAPSODY (n=122)	PTA (n =123)	WRAPSODY (n=112)
Arm / Side of access			
Right	26 / 122 (21.3%)	28 / 123 (22.8%)	30 / 112 (26.8%)
Left	96 / 122 (78.7%)	95 / 123 (77.2%)	82 / 112 (73.2%)
Current Access Position			
Upper arm	113 / 122 (92.6%)	108 / 122 (88.5%)	105 / 112 (93.8%)
Across elbow	8 / 122 (6.6%)	10 / 122 (8.2%)	0 / 112 (0.0%)
Forearm	1 / 122 (0.8%)	4 / 122 (3.3%)	7 / 112 (6.3%)
AVF location			Not applicable
Radiocephalic	2 / 122 (1.6%)	3 / 121 (2.5%)	
Brachiocephalic	89 / 122 (73.0%)	83 / 121 (68.6%)	
Brachiobasilic	31 / 122 (25.4%)	35 / 121 (28.9%)	
AVF transposition			
Transposed	41 / 120 (34.2%)	43 / 121 (35.5%)	
Translocated	1 / 120 (0.8%)	0 / 121 (0.0%)	
Not transposed	78 / 120 (65.0%)	78 / 121 (64.5%)	
AVG material type	Not applicable		
Synthetic			109 / 112 (97.3%)
Biological			3 / 112 (2.7%)
AVG venous anastomosis location			
Axillary			50 / 112 (44.6%)
Basilic			42 / 112 (37.5%)
Brachial			14 / 112 (12.5%)
Cephalic			4 / 112 (3.6%)
Other			2 / 112 (1.8%)
Unknown			0 / 112 (0.0%)
AVG arterial anastomosis location			
Axillary			15 / 112 (13.4%)
Brachial			92 / 112 (82.1%)
Radial			0 / 112 (0.0%)
Ulnar			0 / 112 (0.0%)
Other			1 / 112 (0.9%)
Unknown			4 / 112 (3.6%)
AVG configuration			
Straight			71 / 112 (63.4%)
Looped			41 / 112 (36.6%)

Table 11. Target Lesion Characteristics

Parameter		AVF Cohort		AVG Cohort
		WRAPSODY (n=122)	PTA (n =123)	WRAPSODY (n=112)
Site Assessments				
Proximal RVD[1] (mm)		9.7 ± 2.3 (122)	9.1 ± 1.9 (123)	8.2 ± 1.6 (113)
Distal RVD[1] (mm)		9.5 ± 2.0 (122)	9.2 ± 1.8 (123)	8.0 ± 2.0 (113)
Total Lesion Length (mm)		34.4 ± 20.3 (122)	32.7 ± 23.6 (123)	28.7 ± 21.2 (113)
Number of WRAPSODY CIE Implanted per Subject	1	117 / 122 (95.9%)	n/a	107 / 112 (95.5%)
	2	5 / 122 (4.1%)	n/a	5 / 112 (4.5%)
Type				
De novo		46 / 122 (37.7%)	53 / 123 (43.1%)	53 / 113 (46.9%)
Restenotic		76 / 122 (62.3%)	70 / 123 (56.9%)	60 / 113 (53.1%)
Pre-procedure Diameter Stenosis (%)		75.6 ± 11.8 (122)	75.9 ± 13.4 (123)	75.0 ± 12.6 (113)
Post-procedure Diameter Stenosis (%)		1.93 ± 9.48 (121)	11.8 ± 12.3 (123)	1.68 ± 3.67 (112)
Core Laboratory Assessments				
Target Lesion Vessel				
Axillary Vein		4 / 117 (3.4%)	4 / 117 (3.4%)	34 / 103 (33.0%)
Brachial Vein		1 / 117 (0.9%)	0 / 117 (0.0%)	5 / 103 (4.9%)
Cephalic Vein		77 / 117 (65.8%)	77 / 117 (65.8%)	4 / 103 (3.9%)
Basilic Vein		30 / 117 (25.6%)	30 / 117 (25.6%)	38 / 103 (36.9%)
Subclavian Vein		0 / 117 (0.0%)	2 / 117 (1.7%)	0 / 103 (0.0%)
Brachiocephalic Vein		4 / 117 (3.4%)	2 / 117 (1.7%)	0 / 103 (0.0%)
Other		1 / 117 (0.9%)	2 / 117 (1.7%)	22 / 103 (21.4%)
Stenosis Length (mm)		39.8 ± 15.7 (117)	33.8 ± 17.0 (116)	36.5 ± 18.4 (102)
Pre-Procedure				
Minimum Lumen Diameter		3.6 ± 1.5 (117)	3.7 ± 1.6 (117)	2.9 ± 1.3 (102)
Diameter Stenosis (%)		63.6 ± 12.0 (117)	61.5 ± 12.9 (117)	64.5 ± 13.8 (102)
Post-Procedure				
Minimum Lumen Diameter		8.5 ± 1.9 (112)	7.2 ± 1.6 (82)	7.1 ± 1.1 (112)
Diameter Stenosis (%)		17.4 ± 8.2 (112)	27.8 ± 11.2 (82)	15.4 ± 6.8 (96)

[1] RVD = reference vessel/graft diameter

Table 12. Number of Subjects Implanted per WRAPSODY CIE Size

WRAPSODY CIE Diameter (mm)	Number of Subjects Implanted								
	WRAPSODY CIE Length (mm)								
	30	40	50	60	70	75	80	100	125
AVF Cohort									
6	Not offered		0	Not offered		0	Not offered	0	0
7			0			3		1	0
8			13			4		1	0
9			12			10		4	1
10			15			11		11	0
12	0	6	2	12	0	Not offered	6	Not offered	
14	0	2	4	6	0		0		
16	0	1	0	0	0		2		
AVG Cohort									
6	Not offered		0	Not offered		0	Not offered	0	0
7			11			5		3	0
8			35			19		3	0
9			15			11		3	1
10			7			2		0	0
12	0	0	0	0	0	Not offered	0	Not offered	
14	0	0	1	0	0		1		
16	0	0	0	0	0		0		

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the modified intent to treat (mITT) population of 245 subjects in the AVF cohort and all (112) subjects in the AVG cohort; 240 AVF and 109 AVG subjects were available for the 30-day evaluation. The mITT population includes all subjects as randomized who received treatment. One patient was randomized to treatment with the Wrapsody CIE but did not receive treatment with the WRAPSODY CIE due to procedural complication of extravasation after pre-dilation and randomization that required treatment on an emergent basis with a commercial stent. The primary safety endpoint was freedom from localized or systemic safety events through 30 days that affected the access or venous outflow circuit and resulted in reintervention, hospitalization, or death; specific events of CD-TLR or reintervention due to target lesion thrombosis were counted as failures of primary effectiveness and not included as failures of primary safety. All primary safety events were adjudicated by the CEC. The results for the AVF and AVG cohorts are presented in Table 13 and Table 14, respectively.

In the AVF cohort, the proportion of subjects free from primary safety events was 96.6% in the WRAPSODY arm and 95.0% in the PTA arm and the non-inferiority hypothesis was met ($p < 0.0001$). In the AVG cohort, the proportion of subjects free from primary safety events was 95.4%, which met the performance goal of 89% ($p = 0.0157$). The per protocol (PP) population was prospectively

defined as a secondary analysis population and results were comparable to the mITT population.

In the WRAPSODY arm of the AVF cohort, six safety events occurred in four patients:

- All six events were access circuit non-target lesion revascularizations, including five new lesions and one restenosis. One lesion was treated with PTA and a drug eluting stent, all other lesions were treated with PTA only. All lesions were resolved with functional dialysis access restored.

In the PTA arm of the AVF cohort, seven safety events occurred in six patients:

- Two patients had non-clinically driven target lesion revascularization; both were treated with PTA only and lesions were resolved with functional dialysis access restored.
- Five patients had access circuit non-target lesion revascularization. Three patients had new lesions, one treated with a drug eluting stent and two treated with PTA only; lesions were resolved with functional dialysis access restored. One patient had a restenosis treated with PTA; lesion was resolved with functional dialysis access restored. One patient had both a new lesion and restenosis treated with bare metal stents and thrombectomy in addition to PTA; the dialysis access site was abandoned for this patient.

In the AVG cohort, six safety events occurred in five patients:

- One patient had non-clinically driven target lesion revascularization treated with PTA only; lesion was resolved with functional dialysis access restored.
- Five patients had access circuit non-target lesion revascularization, including three new lesions treated with PTA and two thromboses, one treated with PTA and thrombectomy and one treated with a covered stent and thrombectomy. All lesions were resolved with functional dialysis access restored.

Table 13. AVF Freedom from Localized or Systemic Safety Events[1] through 30 days

Group	Primary Safety Event Rate, n/N (%), [95% CI]		Difference % [95% CI]	Non-inferiority P-value
	WRAPSODY (n=122)	PTA (n =123)		
Modified Intent to Treat[2]	115 / 119 (96.6%) [91.6%, 99.1%]	115 / 121 (95.0%) [89.5%, 98.2%]	1.6% [-3.4%, 6.6%]	< 0.0001†
Per Protocol	112 / 116 (96.6%) [91.4%, 99.1%]	113 / 118 (95.8%) [90.4%, 98.6%]	0.8% [-4.1%, 5.7%]	< 0.0001†

[1] CEC adjudicated

[2] mITT includes all subjects as randomized who received treatment

† Statistically significant, $p < 0.05$

Table 14. AVG Freedom from Localized or Systemic Safety Events[1] through 30 Days

Group	Primary Safety Event Rate n/N (%), [95% CI]	Performance Goal	P-value
	WRAPSODY (n=112)		
Intent to Treat[2]	104 / 109 (95.4%) [89.6%, 98.5%]	89%	0.0157†
Per Protocol	98 / 102 (96.1%) [90.3%, 98.9%]	89%	0.0097†

[1] CEC adjudicated
[2] All subjects enrolled were treated as planned, therefore the ITT and mITT groups are identical
† Statistically significant, $p < 0.05$

Adverse effects that occurred in the PMA clinical study:

Adverse effects are reported in Tables 15-17 for the AVF cohort and Tables 18-20 for the AVG cohort. Separate tables report all reported adverse events, procedure related events, and device related events. Rates were generally similar between the WRAPSODY and PTA arms other than a higher rate of target lesion restenosis reported in the PTA arm. As indicated in the study protocol, device related events were adjudicated by the CEC.

Table 15. AVF All Site-Reported Adverse Events Through 6 Months (210 Days)

Event Type	WRAPSODY		PTA	
	Event Count	Event Rate per Patient, n/N (%)	Event Count	Event Rate per Patient, n/N (%)
Total	158	73 / 122 (59.8%)	247	98 / 123 (79.7%)
Abrupt vessel closure of treated segment (abrupt occlusion)	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Access (puncture) site complication requiring surgery or transfusion	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Amputation	2	2 / 122 (1.6%)	0	0 / 123 (0.0%)
Anemia	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Aneurysm	4	3 / 122 (2.5%)	5	5 / 123 (4.1%)
Angina	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Arterial perforation or rupture	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Atrial fibrillation	3	3 / 122 (2.5%)	1	1 / 123 (0.8%)
Bacteremia or septicemia	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Bleeding complication	2	2 / 122 (1.6%)	4	4 / 123 (3.3%)
Bronchitis or bronchiolitis	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Cardiac arrest	3	3 / 122 (2.5%)	4	4 / 123 (3.3%)
Cardiac arrhythmia	1	1 / 122 (0.8%)	5	3 / 123 (2.4%)
Cardiogenic shock	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Congestive Heart Failure (CHF)	1	1 / 122 (0.8%)	0	0 / 123 (0.0%)
Coronary Artery Disease (CAD)	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Dialysis Access Complications	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Dissection	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Edema, significant	1	1 / 122 (0.8%)	3	3 / 123 (2.4%)
Extravasation of contrast media / Perforation	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Fever (> 38.3ºC/101ºF)	2	2 / 122 (1.6%)	0	0 / 123 (0.0%)
Gastro-intestinal bleeding	1	1 / 122 (0.8%)	0	0 / 123 (0.0%)
Hematoma <5 cm at puncture site	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Hyperglycemia	2	2 / 122 (1.6%)	3	3 / 123 (2.4%)

Event Type	WRAPSODY		PTA	
	Event Count	Event Rate per Patient, n/N (%)	Event Count	Event Rate per Patient, n/N (%)
Hypertension	3	2 / 122 (1.6%)	4	4 / 123 (3.3%)
Hypotension	2	2 / 122 (1.6%)	4	3 / 123 (2.4%)
Infection, localized	4	4 / 122 (3.3%)	4	4 / 123 (3.3%)
Infection, puncture site	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Inflammation	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Myocardial infarction	3	2 / 122 (1.6%)	3	3 / 123 (2.4%)
Myocardial ischemia	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Pain	9	9 / 122 (7.4%)	4	4 / 123 (3.3%)
Pneumonia	3	3 / 122 (2.5%)	3	2 / 123 (1.6%)
Pseudoaneurysm	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Pulmonary edema	2	2 / 122 (1.6%)	0	0 / 123 (0.0%)
Renal failure/renal insufficiency	2	2 / 122 (1.6%)	2	2 / 123 (1.6%)
Respiratory distress	2	2 / 122 (1.6%)	2	2 / 123 (1.6%)
Restenosis (non-target lesion)	28	20 / 122 (16.4%)	25	18 / 123 (14.6%)
Restenosis of treated segment (target lesion)	15	14 / 122 (11.5%)	66	52 / 123 (42.3%)
SARS, COVID-19	3	3 / 122 (2.5%)	2	2 / 123 (1.6%)
Sepsis or systemic infection	4	4 / 122 (3.3%)	0	0 / 123 (0.0%)
Steal syndrome	3	3 / 122 (2.5%)	5	4 / 123 (3.3%)
Stenosis (non-target)	21	19 / 122 (15.6%)	18	17 / 123 (13.8%)
Stroke or other neurological complications	2	2 / 122 (1.6%)	1	1 / 123 (0.8%)
Thrombosis	3	3 / 122 (2.5%)	2	1 / 123 (0.8%)
Total occlusion of the vascular access circuit	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Transient ischemic attack (TIA)	1	1 / 122 (0.8%)	0	0 / 123 (0.0%)
Urinary tract infection (UTI)	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Vascular access complications	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Ventricular tachycardia	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Vessel rupture	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Vessel spasm or recoil	0	0 / 122 (0.0%)	4	4 / 123 (3.3%)
Other event	20	15 / 122 (12.3%)	48	24 / 123 (19.5%)

Table 16. AVF Site-Reported Procedure Related[1] Adverse Events Through 6 Months (210 Days)

Event Type[1]	WRAPSODY		PTA	
	Event Count	Event Rate per Patient, n/N (%)	Event Count	Event Rate per Patient, n/N (%)
Total	11	9 / 122 (7.4%)	41	33 / 123 (26.8%)
Abrupt vessel closure of treated segment (abrupt occlusion)	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Access (puncture) site complication requiring surgery or transfusion	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Arterial perforation or rupture	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Dissection	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Edema, significant	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Extravasation of contrast media / Perforation	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)
Hematoma <5 cm at puncture site	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Inflammation	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Restenosis (non-target lesion)	3	3 / 122 (2.5%)	2	2 / 123 (1.6%)
Restenosis of treated segment (target lesion)	4	4 / 122 (3.3%)	17	17 / 123 (13.8%)
Steal syndrome	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Stenosis (non-target)	1	1 / 122 (0.8%)	1	1 / 123 (0.8%)

Thrombosis	0	0 / 122 (0.0%)	1	1 / 123 (0.8%)
Vascular access complications	1	1 / 122 (0.8%)	0	0 / 123 (0.0%)
Vessel rupture	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)
Vessel spasm or recoil	0	0 / 122 (0.0%)	4	4 / 123 (3.3%)
Other event	1	1 / 122 (0.8%)	3	2 / 123 (1.6%)

[1] Possibly, probably or definitely procedure related according to the investigative site

Table 17. AVF CEC Adjudicated Device Related[1] Adverse Events Through 6 Months (210 Days)

Event Type[1]	WRAPSODY		PTA	
	Event Count	Event Rate per Patient, n/N (%)	Event Count	Event Rate per Patient, n/N (%)
Total	5	4 / 122 (3.3%)	9	9 / 123 (7.3%)
Non-target lesion stenosis (new lesion)	3	2 / 122 (1.6%)	0	0 / 123 (0.0%)
Target lesion restenosis	2	2 / 122 (1.6%)	3	3 / 123 (2.4%)
Vascular Complication (AVF related)[2]	0	0 / 122 (0.0%)	4	4 / 123 (3.3%)
Other[3]	0	0 / 122 (0.0%)	2	2 / 123 (1.6%)

[1] Possibly, probably or definitely device related according to the CEC
[2] Includes events of perforation (2), dissection, and extravasation
[3] Includes events of vessel spasm or recoil and recoil/PTA failure

Table 18. AVG All Site-Reported Adverse Events Through 6 Months (210 Days)

Event Type	Event Count	Event Rate per Patient, n/N (%)
Total	258	77 / 112 (68.8%)
Allergic reaction (medication, contrast media, device, etc.)	1	1 / 112 (0.9%)
Amputation	4	3 / 112 (2.7%)
Anemia	6	3 / 112 (2.7%)
Aneurysm	1	1 / 112 (0.9%)
Angina	4	3 / 112 (2.7%)
Arterial bypass surgery	1	1 / 112 (0.9%)
Atrial fibrillation	1	1 / 112 (0.9%)
Bacteremia or septicemia	5	5 / 112 (4.5%)
Bleeding complication	3	3 / 112 (2.7%)
Bronchitis or bronchiolitis	1	1 / 112 (0.9%)
Cardiac arrest	2	2 / 112 (1.8%)
Cardiac arrhythmia	3	3 / 112 (2.7%)
Dialysis Access Complications	5	3 / 112 (2.7%)
Edema, significant	2	1 / 112 (0.9%)
Fever (> 38.3ºC/101ºF)	1	1 / 112 (0.9%)
Gastro-intestinal bleeding	5	1 / 112 (0.9%)
Hemorrhage, with or without transfusion	1	1 / 112 (0.9%)
Hypertension	6	3 / 112 (2.7%)
Hypotension	2	2 / 112 (1.8%)
Infection, access circuit, stent graft	1	1 / 112 (0.9%)
Infection, localized	6	5 / 112 (4.5%)
Pain	22	8 / 112 (7.1%)
Peripheral ischemia	1	1 / 112 (0.9%)
Pneumonia	3	3 / 112 (2.7%)
Pseudoaneurysm	5	4 / 112 (3.6%)
Pulmonary edema	3	3 / 112 (2.7%)
Renal failure/renal insufficiency	1	1 / 112 (0.9%)

Event Type	Event Count	Event Rate per Patient, n/N (%)
Respiratory arrest	1	1 / 112 (0.9%)
Respiratory distress	3	2 / 112 (1.8%)
Respiratory failure	3	1 / 112 (0.9%)
Restenosis (non-target lesion)	22	13 / 112 (11.6%)
Restenosis of treated segment (target lesion)	7	7 / 112 (6.3%)
SARS, COVID-19	6	6 / 112 (5.4%)
Seizure	1	1 / 112 (0.9%)
Sepsis or systemic infection	6	5 / 112 (4.5%)
Steal syndrome	3	3 / 112 (2.7%)
Stenosis (non-target)	34	23 / 112 (20.5%)
Stroke or other neurological complications	4	4 / 112 (3.6%)
Thrombosis	20	13 / 112 (11.6%)
Total occlusion of the vascular access circuit	1	1 / 112 (0.9%)
Transient ischemic attack (TIA)	1	1 / 112 (0.9%)
Vascular access complications	1	1 / 112 (0.9%)
Vessel rupture	3	3 / 112 (2.7%)
Other event	46	26 / 112 (23.2%)

Table 19. AVG Site-Reported Procedure Related[1] Adverse Events Through 6 Months (210 Days)

Event Type[1]	Event Count	Event Rate per Patient, n/N (%)
Total	24	16 / 112 (14.3%)
Dialysis Access Complications	2	2 / 112 (1.8%)
Edema, significant	2	1 / 112 (0.9%)
Infection, localized	1	1 / 112 (0.9%)
Pseudoaneurysm	3	2 / 112 (1.8%)
Pulmonary edema	1	1 / 112 (0.9%)
Steal syndrome	1	1 / 112 (0.9%)
Stenosis (non-target)	2	2 / 112 (1.8%)
Thrombosis	7	3 / 112 (2.7%)
Total occlusion of the vascular access circuit	1	1 / 112 (0.9%)
Vessel rupture	3	3 / 112 (2.7%)
Other event	1	1 / 112 (0.9%)

[1] Possibly, probably or definitely procedure related according to the investigative site

Table 20. AVG CEC Adjudicated Device Related[1] Adverse Events Through 6 Months (210 Days)

Event Type[1]	Event Count	Event Rate per Patient, n/N (%)
Total	10	9 / 112 (8.0%)
Access Circuit Abandonment	1	1 / 112 (0.9%)
Non-target lesion thrombosis	1	1 / 112 (0.9%)
Target lesion restenosis	1	1 / 112 (0.9%)
Target lesion thrombosis	4	4 / 112 (3.6%)
Vascular Complication (AVG Related)[2]	2	2 / 112 (1.8%)
Other[3]	1	1 / 112 (0.9%)

[1] Possibly, probably or definitely device related according to the CEC

[2] Includes events of pseudoaneurysm (2)

[3] Includes event of steal syndrome

2. Effectiveness Results

The analysis of effectiveness was based on the mITT population including 229 evaluable AVF cohort subjects and 97 evaluable AVG cohort subjects at the 6-month time point. The primary effectiveness endpoint was TLPP at 6 months, defined as freedom from CD-TLR or access circuit thrombosis, and is presented in Table 21 and Table 22 and Figure 5 and Figure 6.

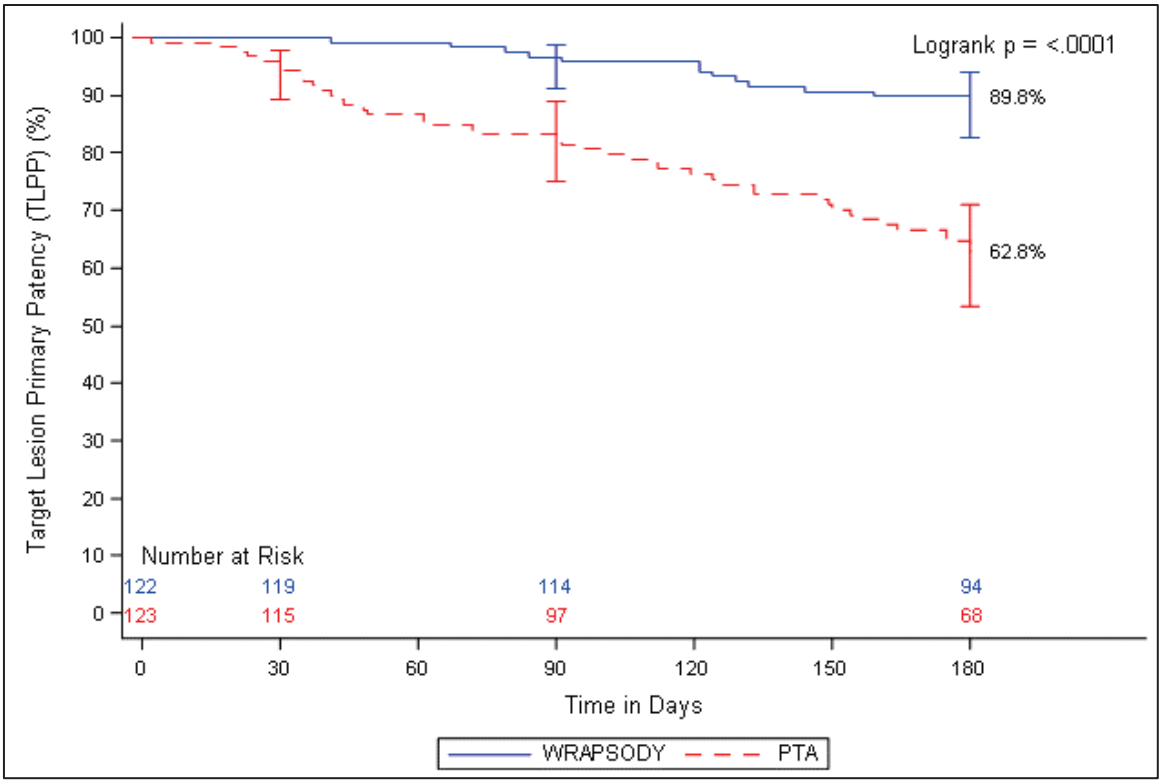
In the AVF cohort, TLPP at 6 months was 90% in the WRAPSODY arm, which was significantly higher than the 62% rate in the PTA arm ($p < 0.0001$). The proportion of subjects with TLPP at 6 months in the AVG cohort was 81%, which was greater than the effectiveness PG of 60% ($p < 0.0001$). Therefore, the primary effectiveness endpoint was met. The PP population was prospectively defined as a secondary analysis population and results were comparable to the mITT population (AVF: 90% vs. 63%, $p < 0.0001$; AVG: 83%, $p < 0.0001$).

Pre-specified Kaplan-Meier time to event analysis was consistent with the primary endpoint analysis at 6 months, indicating 90% TLPP for the WRAPSODY CIE and 63% TLPP for PTA in the AVF cohort (log-rank $p < 0.0001$), and 82% TLPP for the WRAPSODY CIE in the AVG cohort.

Table 21. AVF Target Lesion Primary Patency[1] at 6 Months

Group	WRAPSODY	PTA	Difference (95% CI)[2]	P-value[2]
TLPP – Modified Intent to Treat[2]	103 / 115 (89.6%) (95% CI: 82.5%, 94.5%)	71 / 114 (62.3%) (95% CI: 52.7%, 71.2%)	27.3% (16.8%, 37.8%)	< 0.0001†
Clinically driven target lesion revascularization (CD-TLR)	12 / 115 (10.4%) (95% CI: 5.5%, 17.5%)	43 / 114 (37.7%)	-27.3%	Not Applicable
Target lesion thrombosis	2 / 114 (1.8%) (95% CI: 0.2%, 6.2%)	2 / 111 (1.8%)	-0.0%	
TLPP – Per Protocol[3]	101 / 112 (90.2%) (95% CI: 83.1%, 95.0%)	71 / 112 (63.4%) (95% CI: 53.8%, 72.3%)	26.8% (16.3%, 37.3%)	< 0.0001†
Clinically driven target lesion revascularization (CD-TLR)	11 / 112 (9.8%) (95% CI: 5.0%, 16.9%)	41 / 112 (36.6%)	-26.8%	Not Applicable
Target lesion thrombosis	2 / 111 (1.8%) (95% CI: 0.2%, 6.4%)	2 / 109 (1.8%)	-0.0%	

[1] CEC adjudicated
[2] mITT includes all subjects as randomized who received treatment
[3] PP includes all mITT subjects who additionally met all inclusion/exclusion criteria
† Statistically significant, $p < 0.05$



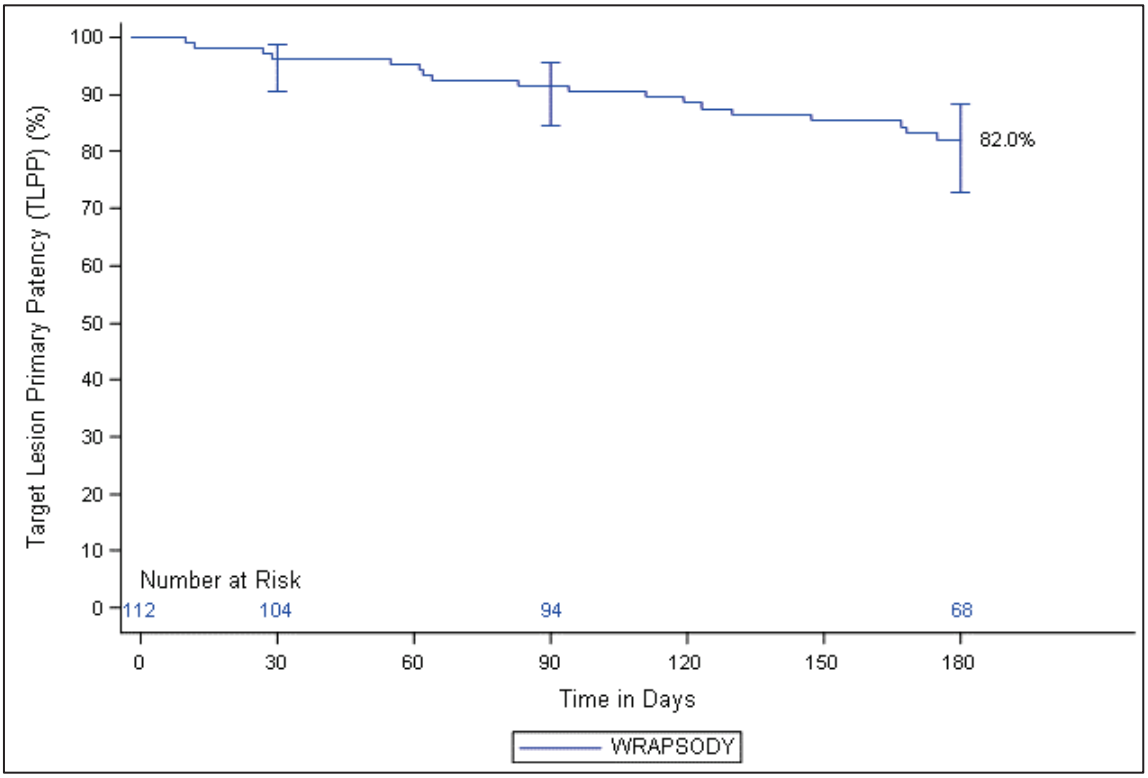
Timepoint	Day 0	Day 30	Day 90	Day 180	Logrank P-value
WRAPSODY					
TLPP (95% CI)	100% (-,-)	100% (-,-)	96.6% (91.3%,98.7%)	89.8% (82.7%,94.0%)	<0.0001
Number with Event	0	0	4	12	
PTA					
TLPP (95% CI)	100% (-,-)	95.0% (89.3%,97.7%)	83.2% (75.2%,88.9%)	62.8% (53.2%,70.9%)	
Number with Event	0	6	20	43	

Figure 5. AVF Kaplan Meier Curve of Target Lesion Primary Patency

Table 22. AVG Target Lesion Primary Patency[1] at 6 Months

Group	WRAPSODY	Performance Goal	P-value[2]
TLPP – Modified Intent to Treat[2]	79 / 97 (81.4%) (95% CI: 72.3%, 88.6%)	60%	< 0.0001†
Clinically driven target lesion revascularization (CD-TLR)	18 / 97 (18.6%)	Not applicable	
Target lesion thrombosis	11 / 94 (11.7%)		
TLPP – Per Protocol[3]	75 / 90 (83.3%) (95% CI: 74.0%, 90.4%)	60%	< 0.0001†
Clinically driven target lesion revascularization (CD-TLR)	15 / 90 (16.7%)	Not applicable	
Target lesion thrombosis	9 / 88 (10.2%)		

[1] CEC adjudicated
[2] mITT includes all subjects as randomized who received treatment
[3] PP includes all mITT subjects who additionally met all inclusion/exclusion criteria
† Statistically significant, $p < 0.05$



Timepoint	Day 0	Day 30	Day 90	Day 180
WRAPSODY				
ACPP (95% CI)	100% -	96.3% (90.5%,98.6%)	91.6% (84.5%,95.6%)	82.0% (72.9%,88.3%)
Number with Event	0	4	9	18

Figure 6. AVG Kaplan Meier Curve of Target Lesion Primary Patency

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: sex, race, age. The primary safety and effectiveness analyses were performed on these subgroups for evaluable subjects and are reported in Table 23 – Table 26. Safety results were generally comparable between groups. For effectiveness, the WRAPSODY CIE continued to have higher TLPP compared to PTA across subgroups. TLPP in the AVF cohort was higher for female compared to male subjects, for African American / black compared to Caucasian / white subjects, and for younger patients compared to older patients in both the WRAPSODY and PTA arms. Similarly, female subjects also had higher TLPP compared to male subjects in the AVG cohort; TLPP by race and age was comparable.

Table 5. AVF Freedom from Localized or Systemic Safety Events Through 30 days by Sex, Race, and Age

Parameter	WRAPSODY	PTA	Difference
Sex			
Male	67 / 68 (98.5%)	64 / 69 (92.8%)	5.8%
Female	48 / 51 (94.1%)	51 / 52 (98.1%)	-4.0%
Race			
Black	46 / 48 (95.8%)	47 / 50 (94.0%)	1.8%
Asian	3 / 3 (100.0%)	6 / 6 (100.0%)	-
Non-Black / Non-Asian	66 / 68 (97.1%)	62 / 65 (95.4%)	1.7%
Age			
≤ Median	59 / 59 (100.0%)	56 / 61 (91.8%)	8.2%
> Median	56 / 60 (93.3%)	59 / 60 (98.3%)	-5.0%

Table 24. AVG Freedom from Localized or Systemic Safety Events Through 30 days by Sex, Race, and Age

Parameter	WRAPSODY
Sex	
Male	45 / 49 (91.8%)
Female	59 / 60 (98.3%)
Race	
Black	64 / 68 (94.1%)
Asian	3 / 3 (100.0%)
Non-Black / Non-Asian	37 / 38 (97.4%)
Age	
≤ Median	52 / 55 (94.5%)
> Median	52 / 54 (96.3%)

Table 25. AVF Target Lesion Primary Patency at 6 Months by Sex, Race, and Age

Parameter	WRAPSODY	PTA	Difference
Sex			
Male	57 / 66 (86.4%)	37 / 65 (56.9%)	29.4%
Female	46 / 49 (93.9%)	34 / 49 (69.4%)	24.5%
Race			
Black	44 / 46 (95.7%)	33 / 48 (68.8%)	26.9%
Asian	3 / 3 (100.0%)	4 / 4 (100.0%)	-
Non-Black / Non-Asian	56 / 66 (84.8%)	34 / 62 (54.8%)	30.0%
Age			
≤ Median	55 / 58 (94.8%)	40 / 60 (66.7%)	28.2%
> Median	48 / 57 (84.2%)	31 / 54 (57.4%)	26.8%

Table 26. AVG Target Lesion Primary Patency at 6 Months by Sex, Race, and Age

Parameter	WRAPSODY
Sex	
Male	32 / 42 (76.2%)
Female	47 / 55 (85.5%)
Race	
Black	49 / 61 (80.3%)
Asian	2 / 2 (100.0%)
Non-Black / Non-Asian	28 / 34 (82.4%)
Age	
≤ Median	40 / 49 (81.6%)
> Median	39 / 48 (81.3%)

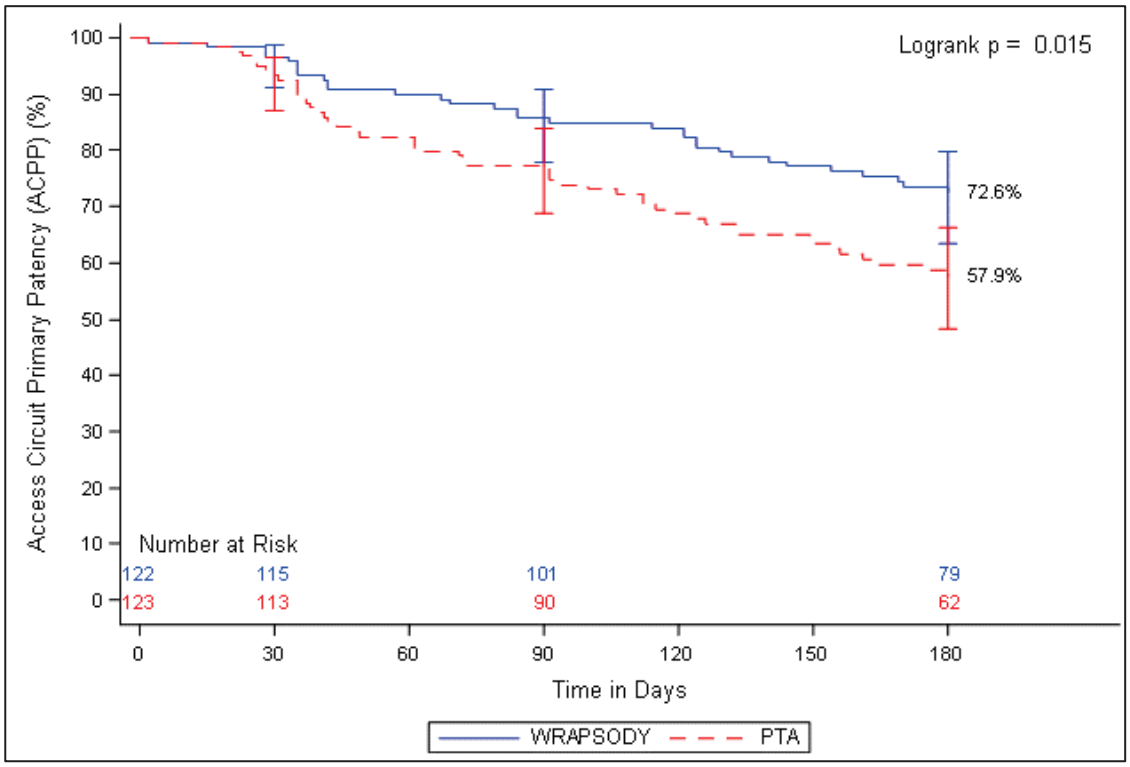
4. Secondary and Other Endpoints

   Access circuit primary patency (ACPP) is an important effectiveness endpoint evaluated in this study and is defined as time to any venous outflow circuit re-intervention or access thrombosis or abandonment; ACPP is inclusive of all patency events, including those that occurred at the target lesion (i.e. inclusive of TLPP). In the AVF cohort, ACPP for the WRAPSODY arm was 72% at 6 months compared to 57% in the PTA arm (p = 0.016) (Table 27). ACPP in the AVG cohort was 68% at 6 months (Table 28). As specified in the statistical analysis plan, supplemental analyses were conducted using the Kaplan-Meier method. Figure 7 and Figure 8 show the Kaplan-Meier curves for the ACPP endpoint through 6 months in the AVF and AVG cohorts, respectively. The Kaplan-Meier rates were consistent, indicating 73% ACPP for the WRAPSODY CIE and 58% ACPP for PTA in the AVF cohort (log-rank p = 0.015), and 69% ACPP for the WRAPSODY CIE in the AVG cohort. Through 6 months, reintervention was required for inflow circuit lesions in two additional patients in the WRAPSODY arm of the AVF cohort and three additional patients in the AVG cohort.

Table27. AVF Access Circuit Primary Patency (mITT Subjects)

Endpoint	n/N (%) (95% CI)[1]			
	WRAPSODY	PTA	Difference (95% CI)[2]	P-value[2]
Access Circuit Primary Patency (ACPP) at 6 months (180 days)	83 / 115 (72.2%) (63.0%, 80.1%)	65 / 114 (57.0%) (47.4%, 66.3%)	15.2% (2.9%, 27.4%)	0.016

[1] Exact 95% confidence intervals.
[2] P-value from the Z-test for the difference in proportions with pooled variance (two-group chi-square test equivalent). Confidence interval from the corresponding normal approximation.



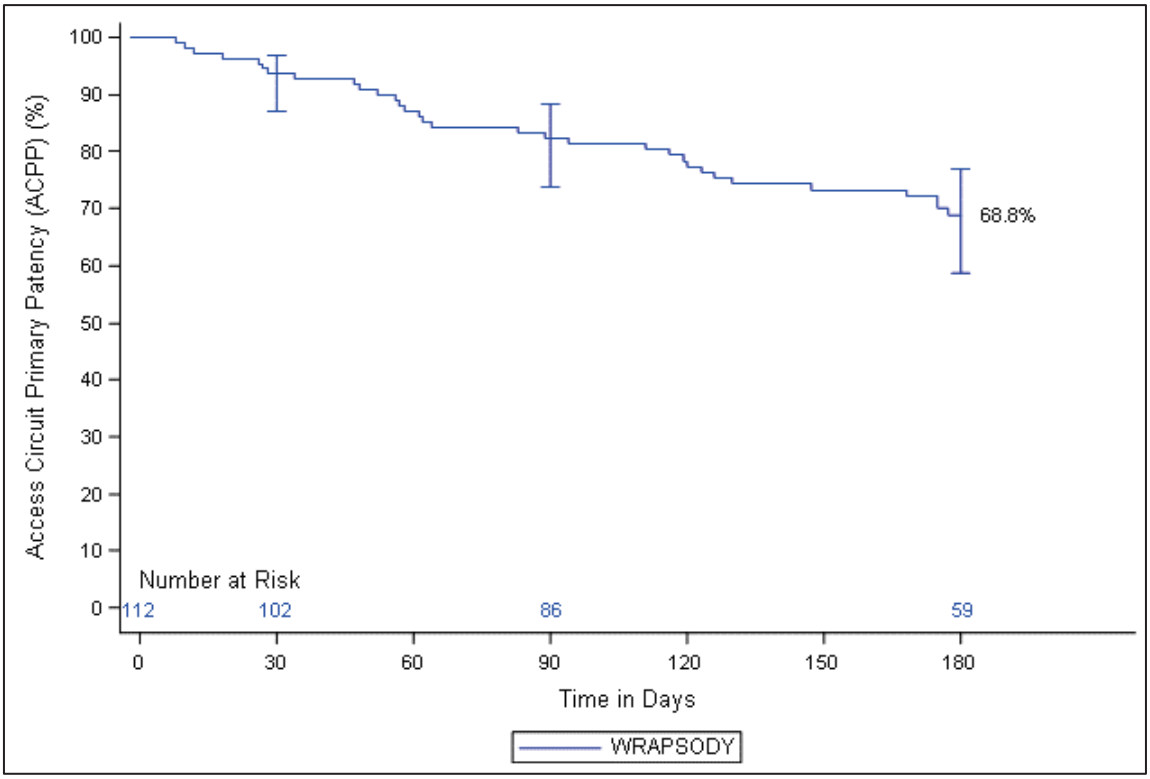
Timepoint	Day 0	Day 30	Day 90	Day 180	Logrank P-value
WRAPSODY					0.015
Survival (95% CI)	100% (-,-)	96.6% (91.3%,98.7%)	85.7% (78.0%,90.9%)	72.6% (63.5%,79.8%)	
Number with Event	0	4	17	32	
PTA					
Survival (95% CI)	100% (-,-)	93.4% (87.2%,96.6%)	77.4% (68.8%,83.9%)	57.9% (48.3%,66.3%)	
Number with Event	0	8	27	49	

Figure 7. AVF Kaplan Meier Curve of Access Circuit Primary Patency

Table 28. AVG Access Circuit Primary Patency (mITT Subjects)

Endpoint	n/N (%) (95% CI)[1] WRAPSODY
ACPP at 6 months (180 days)	68 / 100 (68.0%) (57.9%, 77.0%)

[1] Exact 95% confidence intervals.



Timepoint	Day 0	Day 30	Day 90	Day 180
WRAPSODY				
ACPP (95% CI)	100% -	93.6% (87.0%,96.9%)	82.4% (73.8%,88.4%)	68.8% (58.7%,76.8%)
Number with Event	0	7	19	32

Figure 8. AVG Kaplan Meier Curve of Access Circuit Primary Patency

Other secondary outcomes evaluated include:

- Assisted target lesion primary patency (aTLPP) defined as time to from post-procedure until uncorrectable target lesion occlusion.
- Post-procedure secondary patency defined as the interval post-procedure until access circuit abandonment.
- Rate of SAEs and rate of SAEs involving the AV access circuit.
- Rate of device observations and potential malfunctions or failures.

- Number of target lesion reinterventions to maintain target lesion patency and number of access circuit interventions to maintain access circuit patency.
- Device success defined as successful delivery to the target lesion, deployment and retrieval of delivery system at index procedure; and procedure success defined as at least one indicator of hemodynamic success in the absence of peri-procedural serious adverse device effects.
- Index of patency function defined as time from initial study procedure to complete access abandonment divided by number of venous outflow circuit reinterventions to maintain hemodialysis.
- Clinical success defined as the resumption of successful dialysis through existing access for at least one session following initial study procedure.

These results are reported in Table 29 for the AVF cohort and Table 30 for the AVG cohort.

Table 29. AVF Other Secondary Outcomes

	WRAPSODY	PTA
Post-procedure secondary patency through 6 months (Kaplan-Meier estimate)	100%	100%
Rate of SAEs through 6 months	38 / 122 (31.1%) (95% CI: 23.1%, 40.2%)	45 / 123 (36.6%) (95% CI: 28.1%, 45.7%)
Rate of SAEs involving the AV access circuit through 6 months	4 / 114 (3.5) (95% CI: 1.0%, 8.7%)	5 / 110 (4.5) (95% CI: 1.5%, 10.3%)
Number of target lesion reinterventions to maintain target lesion patency through 6 months	0.18 ± 0.51 (115) (95% CI: 0.09,0.28) (Range: 0 to 3)	0.47 ± 0.65 (114) (95% CI: 0.35,0.60) (Range: 0 to 3)
Number of interventions to maintain access circuit patency through 6 months	0.48 ± 0.91 (115) (95% CI: 0.31,0.65) (Range: 0 to 5)	0.78 ± 1.12 (114) (95% CI: 0.57,0.99) (Range: 0 to 6)
Device success	120 / 122 (98.4%)[1] (95% CI: 94.2%, 99.8%)	-
Procedure success	121 / 122 (99.2%)[1] (95% CI: 95.5%, 100%)	123 / 123 (100.0%) (95% CI: 97.0%, 100%)

[1] The failures of device and procedure success were associated with inaccurate deployment

Table 30. AVG Other Secondary Outcomes through 6 Months

	WRAPSODY
Post-procedure secondary patency through 6 months (Kaplan-Meier estimate)	95.0% (95% CI: 88.4%,97.9%)
Rate of SAE through 24 months	50 / 112 (44.6%) (95% CI: 35.2%, 54.3%)
Rate of SAE involving the AV access circuit through 6 months	6 / 95 (6.3) (95% CI: 2.4%, 13.2%)
Number of target lesion reinterventions to maintain target lesion patency	0.19 ± 0.42 (97) (95% CI: 0.10,0.27) (Range: 0 to 2)
Number of interventions to maintain access circuit patency	0.26 ± 0.71 (98) (95% CI: 0.11,0.40) (Range: 0 to 5)
Device success	112 / 112 (100.0%) (95% CI: 96.8%, 100.0%)
Procedure success	112 / 112 (100.0%) (95% CI: 96.8%, 100.0%)

5. Device Related Serious Adverse Events and Deaths

   There were no device related serious adverse events in the AVF cohort as adjudicated by the CEC. There was a single device related serious adverse event of access circuit abandonment in the AVG cohort as adjudicated by the CEC.

   A total of 36 deaths were reported in the AVF cohort, 14 in the WRAPSODY arm and 22 in the PTA arm. No deaths were adjudicated by the CEC as related to the study device or procedure. One death in the PTA arm was adjudicated as possibly related to the procedure. A total of 15 deaths were reported in the AVG cohort and none were adjudicated as related to the study device or procedure. Deaths were typically determined to be cardiovascular related, with general causes including cardiac/cardiopulmonary arrest, sepsis, and renal failure.

6. Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 154 investigators of which none were full-time or part-time employees of the sponsor and one had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 1
- Significant payment of other sorts: 0
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

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

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The WRAPSODY FIRST clinical study was a prospective, observational first in human study to evaluate the safety and effectiveness of the WRAPSODY® Cell-Impermeable Endoprosthesis in the treatment of arteriovenous fistula and arteriovenous graft access circuit stenosis. Results from the study have been published (Gilbert, et al., Cardiovascular Interventional Radiology, 2021). A total of 46 subjects were prospectively enrolled at 3 sites in Europe and 62 WRAPSODY CIE devices were implanted. Treatment sites included the peripheral outflow veins (e.g. cephalic arch, basilic vein swing point), the graft-vein anastomosis, and the central veins (up to, but not including the Superior Vena Cava (SVC)). Key inclusion/exclusion criteria can be found in the publication.

Follow-up was scheduled at 1, 3, 6, and 12 months and is complete. An independent data monitoring/clinical event committee adjudicated all reinterventions and device/procedure-relatedness for adverse events.

Of the 46 subjects enrolled, 16 were treated for AVF peripheral vein lesions, 9 for AVG anastomotic lesions, 10 for AVG peripheral lesions, and 11 for AVF/AVG central vein lesions. Overall, 43% of subjects were < 65 years of age, 24/46 were female, mean BMI was 28 ± 6.6, 84.8% were white, 8.7% black, 4.3% Asian, and 2.2% multi-racial; major comorbidities included diabetes mellitus (37%), dyslipidemia (26%), hypertension (48%), and current or former smoking (43%). Average lesion diameter was 7.8 ± 2.3 mm (excluding central vein lesions), average lesion length was 34.2 ± 17.4 mm, mean stenosis % was 70.6% ± 11.1%, and 52.2% of lesions were de novo.

The primary safety endpoint, defined as the proportion of subjects without any localized or systemic safety events that affected the access or venous outflow circuit and resulted in surgery, hospitalization, or death through 30 days, was 97.8% (45/46). The primary effectiveness endpoint, defined as the proportion of subjects with TLPP at 30 days, was 100% (45/45). Procedural success was achieved in all cases (100%; 46/46). Six adverse events had either a relationship to the study device and/or procedure. TLPP, assisted TLPP, ACPP, and assisted ACPP are summarized in Table 31.

Table 31. TLPP, Assisted TLPP, ACPP, and Assisted ACPP

Measure	Timepoint	Overall	AVF Peripheral	AVG Peripheral	AVG Anastamosis	AVF/AVG Central
TLPP	30 days	100% (45/45)	-			
	6 months	97.7% (42/43)				
	12 months	84.6% (33/39)	78.6% (11/14)	77.8% (7/9)	85.7% (6/7)	100% (9/9)
Assisted TLPP	30 days	100% (45/45)	-			
	6 months	100% (43/43)				
	12 months	100% (39/39)				
ACPP	30 days	95.6% (43/45)				
	6 months	84.4% (38/45)				
	12 months	65.9% (29/44)	66.7% (10/15)	70.0% (7/10)	62.5% (5/8)	63.6% (7/11)
Assisted ACPP	30 days	100% (45/45)	-			
	6 months	95.6% (43/45)				
	12 months	88.6% (39/44)				

In conclusion, the results from the WRAPSODY FIRST clinical study further support the safety and effectiveness of the WRAPSODY® Cell-Impermeable Endoprosthesis.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Acute Device Success was achieved for the WRAPSODY CIE in 98.4% and 100% of the subjects in the AVF and AVG cohorts, respectively. Procedure Success associated with evidence of restored hemodynamic flow was achieved in 99.2% of the WRAPSODY subjects in the AVF cohort and 100% of the AVG cohort subjects. For subjects with available follow-up, at least one successful dialysis session using the existing vascular access (i.e., Clinical Success) was achieved in 100% and 99.1% of the WRAPSODY subjects in the AVF and AVG cohort, respectively.

In the AVF cohort, the primary effectiveness endpoint of TLPP through 6 months was significantly higher in subjects treated with the WRAPSODY CIE compared to subjects receiving PTA (89.6% vs. 62.3%, $p<0.0001$). The 6-month TLPP rate for the WRAPSODY CIE in the AVG cohort was 81.4%, and this rate compares favorably to the established performance goal of 60% ($p<0.0001$). Furthermore, this significant improvement in primary patency extended to the entire access circuit, with a 6-month ACPP rate of 72.2% in the WRAPSODY arm of the AVF cohort as compared to 57.0% for PTA ($p=0.016$). A high 6-month ACPP rate of 68.0% was also observed in the

WRAPSODY AVG cohort. The need for target lesion and access circuit reinterventions through 6 months was also reduced with the WRAPSODY CIE compared to PTA. Secondary patency was maintained in 100% of all AVF cohort subjects (treatment and control) and 95% of the AVG cohort subjects through 6 months. These data demonstrate the impact of WRAPSODY CIE treatment on not only the target lesion, but also improved overall access circuit performance and outcomes for this vulnerable population.

Effectiveness of the WRAPSODY CIE was consistent across sex, race, and age. The overall clinical results provide a reasonable assurance of the effectiveness of the WRAPSODY CIE for the proposed indication.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and/or animal studies as well as data collected in a clinical study conducted to support PMA approval as described above.

The primary safety endpoint evaluated freedom from local or systemic safety events affecting either the access or venous outflow circuit within 30 days of index treatment. In the AVF cohort, primary safety in the WRAPSODY arm was found to be non-inferior to the PTA arm (96.6% vs. 95.0%, $p<0.0001$). In the AVG cohort, 95.4% of patients exhibited freedom from safety events, thereby meeting the performance goal of 89% ($p=0.0162$).

A total of 36 deaths were reported in the AVF cohort (14 in the WRAPSODY arm and 22 in the PTA arm) and none of the deaths were considered to be related to the study device; one death in the PTA arm was adjudicated as possibly procedure related. A total of 15 deaths were reported in the AVG cohort and none were considered to be related to the study device or procedure.

In the AVF cohort, for the treatment group, a total of 23 adverse events were indicated by the investigative sites as device related and 11 were indicated as procedure related through 6 months. These events are provided in Tables 16 - 17 and Tables 19 - 20. Similarly, in the AVG cohort, a total of 28 and 24 events were indicated by the investigative sites as device and procedure related, respectively, through 6 months. These events do not impact the safety profile of the WRAPSODY CIE.

The overall clinical results provide a reasonable assurance of the safety of the WRAPSODY CIE for the proposed indication.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The probable benefit of using the WRAPSODY CIE in hemodialysis patients to treat stenosis or occlusion within the dialysis access outflow circuit in the peripheral veins of individuals with an arteriovenous (AV) fistula and at the venous anastomosis of a synthetic AV graft is improved target

lesion primary patency (TLPP) and access circuit primary patency (ACPP) through 6 months. The likelihood of a patient experiencing a benefit is high, based on the TLPP rate of 89.6% at 6 months compared to 62.3% in the PTA arm and the ACPP rate of 72.2% at 6 months compared to 57.0% in the PTA arm in the AVF cohort. In the AVG cohort, TLPP at 6 months was 81.4% and ACPP was 68.0%, comparing favorably to the performance goals. The number of reinterventions needed to sustain these patency rates was notably low for the patients treated with the WRAPSODY CIE in both cohorts.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The proportion of subjects free from primary safety events was 96.6% in subjects treated with the WRAPSODY CIE as compared to 95.0% in subjects treated with PTA alone in the AVF cohort. Similarly, in the AVG cohort, the proportion of subjects free from primary safety events was 95.4% in subjects treated with the WRAPSODY CIE.

1. Patient Perspective

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

In conclusion, given the available information above, the data support that for use in hemodialysis patients for the treatment of stenosis or occlusion within the dialysis access outflow circuit, including stenosis or occlusion:

- in the peripheral veins of individuals with an arteriovenous (AV) fistula,
- at the venous anastomosis of a synthetic AV graft.

the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The results of the WRAPSODY WAVE study demonstrate safety and effectiveness in hemodialysis patients for treatment of stenosis or occlusion within the dialysis access outflow circuit in the peripheral veins of individuals with an arteriovenous (AV) fistula and at the venous anastomosis of a synthetic AV graft. The benefits of the use of the WRAPSODY CIE include superior TLPP and ACPP at 6 months compared to PTA in AVF patients, and favorable TLPP and ACPP compared to literature-derived performance goals in AVG patients. The need for target lesion and access circuit reinterventions through 6 months was also reduced with the WRAPSODY CIE compared to PTA. The benefits in improved TLPP and ACPP are clinically meaningful and were achieved with no added risk of safety events through 30 days when considered in the context of known risks of PTA alone.

XIV. CDRH DECISION

CDRH issued an approval order on December 19, 2024. The final clinical conditions of approval cited in the approval order are described below.

1. Completion of WAVE Study: This is a prospective, multicenter study that includes continued follow-up of the previously enrolled 374 IDE subjects at 43 sites. The purpose of the study is to evaluate the long-term safety and effectiveness of the Merit WRAPSODY® Endovascular Stent Graft. All subjects remaining in the study will continue to be followed through 24 months. Clinical outcomes at 12- and 24-months will include target lesion primary patency (TLPP), assisted target lesion primary patency (aTLPP), access circuit primary patency (ACPP), secondary patency, procedure- and device-related adverse events, number of target lesion reinterventions, number of reinterventions to maintain access circuit patency, percentage of subjects with device and procedural success, index of patency function, and clinical success. Rate of serious adverse events and device observations and potential malfunctions will be evaluated at 12-, 18-, and 24-months. With the exception of TLPP and ACPP at 12 and 24 months, which are key effectiveness endpoints with hypothesis testing, all endpoints will be analyzed descriptively.

2. WRAP Registry: This is a prospective, multi-center, observational registry study to evaluate the safety and effectiveness of the Merit WRAPSODY® Cell Impermeable Endoprosthesis in the long term and under real-world conditions. The study will enroll 250 subjects in up to 25 centers in the US and Canada, with a minimum of 125 subjects enrolled at up to 15 US sites. In addition, the study will have a minimum of 100 evaluable subjects at 36-months post implantation. Clinical outcomes at 6-, 12-, 24-, and-36 months will include target lesion primary patency (TLPP), assisted target lesion primary patency (aTLPP), access circuit primary patency (ACPP), secondary patency, rate of serious adverse events, number of target lesion reinterventions, and number of reinterventions to maintain access circuit patency. Rates of procedure- and device-related adverse events and rate of device observations and potential malfunctions will be evaluated at index procedure, 30 days, and 6-, 12-, 24-, and 36-months. The percentage of subjects with device, procedural success, and anatomic success (< 30% residual stenosis) at index procedure will also be evaluated. All endpoints will be analyzed descriptively.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

1. Gilbert J et al., First Clinical Results of the Merit WRAPSODY™ Cell-Impermeable Endoprosthesis for Treatment of Access Circuit Stenosis in Haemodialysis Patients. Cardiovasc Intervent Radiol. 2021;44(12):1916-1917.