EN Instructions for Use

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℞ Only

1.0 OVERVIEW OF THE AMDS HYBRID PROSTHESIS

1.1 INTENDED USE

The AMDS™ Hybrid Prosthesis (AMDS) is intended for use in combination with standard surgical hemiarch repair for the treatment of patients with acute DeBakey Type I aortic dissections to re-expand the intimal flap within the ascending aorta and encourage positive remodeling through the aortic arch and descending aorta in patients with malperfusion.

1.2 DEVICE DESCRIPTION

AMDS is an implantable, uncovered stent constructed from braided Nitinol wire, attached proximally to a polytetrafluoroethylene (PTFE) felt cuff with polyester (PET) suture (***Figure 1***), which is mounted on a single-use Delivery System using an expanded polytetrafluoroethylene (ePTFE) suture (***Figure 2***).The delivery system consists of a catheter shaft with a pigtail tip that can accommodate insertion of a 0.035" guidewire through the port at the proximal handle. The stent is compressed to the diameter of the catheter shaft, and constrained just proximal to the delivery system tip by:

- An ePTFE suture which is circumferentially knotted around the entire length of the stent to stabilize the stent on the catheter. The ePTFE suture is passed through a skive in the catheter lumen and connected to the green cap (deployment mechanism),
- A clear, protective sheath located on the proximal end of the stent near the cuff, to reduce the profile of the proximal stent for atraumatic insertion of the AMDS system into the transected aorta, which is removed immediately upon stent insertion.

The ePTFE suture constrains the stent during implantation; the green cap is pulled to deploy the stent (proximally, then distally) at the time of implantation. The red cap is non-functional. The AMDS is packaged in a sealed Tyvek® tray within a single unit carton, and provided sterile (Ethylene Oxide), non-pyrogenic, for single use only.

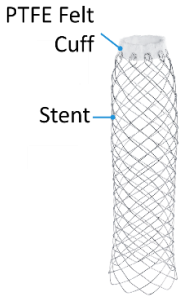

Figure 1. AMDS Stent

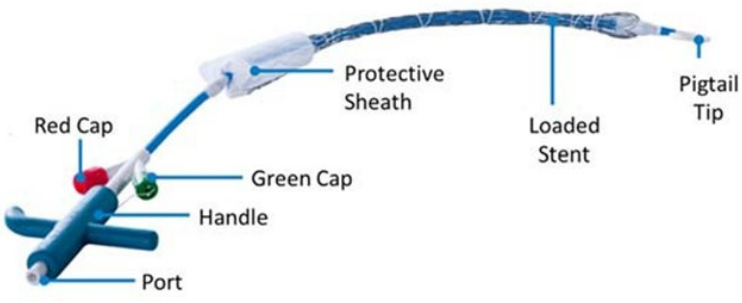

Figure 2. AMDS Delivery System

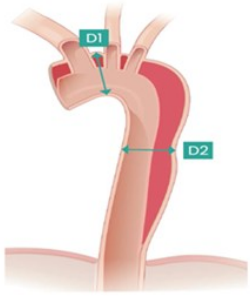

Figure 3. AMDS Sizing

The AMDS uses the uncovered stent component of the device implanted distal to the aortic anastomosis, to expand the true lumen and support the intimal flap, with the goal of promoting remodeling in the aortic arch. In addition, the stent is intended to expand the true lumen and improve the blood flow through the aorta and its tributaries. The AMDS cuff is used to strengthen the distal aortic anastomosis created between a conventional polyester graft and the transected aorta. The main function of the AMDS cuff is to assist in closing the false lumen at the site of the conventional graft to the aorta anastomosis. The entire procedure is performed utilizing an open chest approach while on cardiopulmonary bypass.

The AMDS device is offered in eight configurations based on the stent sizing to fit a range of aortic diameters and lengths (see ***Table 1***). The AMDS stent is available in four straight models (diameters of 40mm and 55mm) and four tapered models (stent diameters tapered from 40mm to 30mm and 55mm to 40mm). The PTFE felt cuff is available in three diameters (24mm diameter for AMDS40 and AMDS4030; 28mm diameter for AMDS40c, AMDS4030c, AMDS55c, and AMDS5540c; and 32mm diameter for AMDS55 and AMDS5540). The AMDS stent is a braided design, resulting in its length being a function of its expanded diameter (i.e. the device lengthens or shortens as its diameter is reduced or increased). The AMDS has an expanded stent free surface area of >95% in all indicated aorta diameters.

Table 1. The AMDS Stent Sizing and Catheter Length

REF	Stent Shape	Aortic Diameter Stent Sizing		Aortic Length Stent Sizing		Cuff Diameter (mm)	Catheter Length (mm)	Minimum Deployment Suture Length (cm)
		D1 Proximal Diameter (mm)	D2 Distal Diameter (mm)	Stent Min Length (mm)*	Stent Max Length (mm)**			
AMDS40	Straight	20-35	25-35	153	207	24	527	135
AMDS40c						28		
AMDS4030	Tapered		20-24	159	203	24		
AMDS4030c						28		
AMDS55	Straight	36-45	36-45	187	215	32	565	150
AMDS55c						28		
AMDS5540	Tapered		27-35	185	211	32	546	145
AMDS5540c						28		

* Represents the minimum stent length when stent is expanded to the largest indicated aorta diameter
** Represents the maximum stent length when stent is expanded to the smallest indicated aorta diameter

2.0 INDICATIONS FOR USE

The AMDS Hybrid Prosthesis is indicated for use in patients with acute DeBakey Type I aortic dissections with malperfusion (including cerebral, visceral, renal, and peripheral malperfusion) and a primary entry tear within the ascending aorta proximal to the innominate artery, who are undergoing open surgical repair within 0-14 days of diagnosis.

3.0 CONTRAINDICATIONS

The AMDS Hybrid Prosthesis is contraindicated in the following:

- Patients who exhibit sensitivity to the implant materials (Polytetrafluoroethylene [PTFE] or Nitinol [e.g., Nickel or Titanium])
- Patients with mycotic aneurysms, aortic fistulous communication with non-vascular structures, uncontrolled systemic infection

4.0 WARNINGS

- **Professional use only.** The AMDS procedure shall only be performed by physicians trained in cardiac surgery and hemiarch repair. Device sizing must be selected by the physician based on the patient-specific anatomy, utilizing guidelines provided in the AMDS Sizing Chart in ***Table 1*****.** Sizing must be based on measurement of the outer aortic diameter (adventitia to adventitia) based on preoperative imaging. Implantation of the AMDS in anatomy beyond the recommended guidelines may result in patient injury or death. The device has not been studied in patients with a primary entry tear located distal to the innominate artery.
- **For single use only. DO NOT reuse, reprocess, or re-sterilize.** Reuse, reprocessing or re-sterilization may compromise the structural integrity of the device and/or lead to device failure which may result in deterioration of health or death of patients. Reuse, reprocessing or re-sterilization may lead to contamination of the device and/or cause patient infection or transmission of infectious disease leading to injury, illness or death of the patient or user.
- **DO NOT** use the device if the labeled expiration date has passed, the packaging is opened or damaged, or the product has been dropped, damaged, or otherwise inappropriately handled. The tray must be intact at the time of use; damage to the seal renders the AMDS non-sterile. If the device or packaging is damaged, return the product to the manufacturer.
- **DO NOT** use the AMDS device in pediatric patients.
- **DO NOT** use a clamp on the PTFE Felt Cuff, Stent, or Delivery System. Clamping may damage the device and result in patient injury.
- **DO NOT** cut the AMDS stent wires; due to the braided wire design, cutting a wire within the stent may cause stent malfunction or vascular damage.
- **DO NOT** deploy the AMDS in the false lumen of the aortic dissection.
- **DO NOT** preclot; the AMDS device; the PTFE felt collar does not require pre-clotting.
- **DO NOT** oversize. Some degree of oversizing is inherently built into the sizing guidance as device selection is based on total aortic diameter adventitia-to-adventitia, while the native true lumen is known to be smaller than this. Device sizing must be selected by the physician based on the patient-specific anatomy, according to the AMDS Sizing Chart in ***Table 1***. Sizing must be based on measurement of the outer aortic diameter (adventitia to adventitia) based on preoperative CT scan imaging. Implantation of the AMDS in anatomy beyond the sizing recommendations (e.g., oversizing) may result in unexpected device conformability (such as stent narrowing).

5.0 PRECAUTIONS

- Physicians should exercise discretion during patient selection for treatment with the AMDS device. Patients with secondary entry tears may present challenging deployment where there is an opportunity for the AMDS to mis-deploy or malposition within the false lumen.
- The AMDS cuff should not be used as a graft to replace the aorta. The AMDS cuff is solely used to buttress and strengthen the anastomosis between the polyester graft and the aorta.
- Differences between the diameter of the AMDS cuff and the diameter of the transected aorta are expected due to the broad range of aortic diameters covered. Malalignment when creating this anastomosis may result in gaps or folds in aortic tissue leading to continued pulsatile flow into the false lumen and/or twisting of the AMDS device.
- Use care to not cut the deployment suture.
- If the AMDS stent is inadvertently mis-deployed in an undesired position within the true lumen, the physician may consider carefully removing the AMDS stent by cutting the tacking sutures and slowly pulling the AMDS stent from the aorta. Withdrawal of the AMDS stent after deployment may lead to vascular damage. A new AMDS stent may then be implanted, taking care to deploy the stent in the desired location. See §13.0, Summary of Clinical Studies and Clinical Benefit for information related to occurrence of mis-deployment in the AMDS clinicals studies.
- Extensive thrombus or calcification in the aortic arch may increase the risk of stroke.
- Excessive aortic tortuosity may preclude safe passage of the device within the aorta.
- Pregnant or breastfeeding women need to be counseled on the radiation risks associated with follow-up CT scans.
- The long-term performance of the AMDS has not yet been established; therefore, patients should be monitored on a regular basis for adverse events, for example false lumen growth.
- The safety and effectiveness of the AMDS has not been clinically studied for use in patients with connective tissue disorders, or subacute or chronic dissections (>14 days after the index event).
- A conventional aortic graft must be anastomosed to the aorta and the conventional graft, aortic wall and the PTFE felt must be incorporated in each suture bite. DO NOT apply tension to the AMDS cuff or proximal graft while suturing the anastomosis, as this may result in stent malposition. When completing the proximal anastomosis, leave the ascending graft long enough to avoid putting tension on the AMDS at the distal anastomosis.
- Device not studied in combination with other hybrid or endovascular stents (e.g., TEVAR endovascular stent).
- The AMDS has not been tested to establish potential of genetic toxicity. Prolonged exposure to genetic toxicants may lead to long term mutagenic and carcinogenic affects. The risks of these potential harms from the product have not been established clinically.

6.0 POTENTIAL ADVERSE EVENTS AND UNDESIRABLE SIDE EFFECTS

Potential adverse effects associated with the hemiarch repair procedure with the use of the AMDS device include, but are not limited to:

- Allergic reaction to device, contrast media, or antithrombotic agents administered during the procedure
- Aortic enlargement or rupture, dissection, perforation or other disease progression requiring future total arch replacement
- Cardiac complication or failure (e.g., arrhythmia, fast heartbeat, cardiac tamponade, heart attack, irregular blood pressure)
- Complications at the surgical site (e.g., infection, fever, pain, or inflammation), hemorrhage and/or bleeding, fistula
- Distal anastomotic new entry (DANE) tears leading to persistent malperfusion or requiring re-operation
- Distal stent-induced new entry tears (dSINE) leading to aortic dissection or requiring reoperation
- Death
- Occlusion, stenosis, thrombosis, thromboembolism, and/or pseudoaneurysm (arterial or venous)
- Post-operative malperfusion leading to multi-system organ failure, limb amputation, or death
- Pulmonary complications (e.g., edema, embolism, pneumonia, respiratory failure)
- Neurological, local, or systemic complications (e.g., stroke, transient ischemic attack (TIA), neuropathy, or spinal cord injury with possible paralysis).
- Visceral ischemia or gastrointestinal symptoms (e.g., nausea/vomiting, liver failure, renal insufficiency)
- Patients may become unstable under hypothermic circulatory arrest during cardiac procedures

Potential adverse effects that may be associated with the AMDS procedure include, but are not limited to:

- Exposure to contrast media and/or radiation during follow-up visits to visualize the AMDS stent
- Malposition of the AMDS stent in the false lumen of the aorta leading to required reintervention
- Potential difficulties in accessing the arch branch vessels during future interventional procedures
- Overly tortuous arch anatomy, leading to incomplete stent expansion in sections of the aorta

7.0 MAGNETIC RESONANCE IMAGING SAFETY AND COMPATIBILITY INFORMATION

A patient with an AMDS implant can be scanned safely in an MR system under the following conditions. Failure to follow these conditions may result in injury. If information about a specific parameter is not included, there are no conditions associated with that parameter.

MR CONDITIONAL

Static Magnetic Field Strength (B_0)	1.5-T or 3-T
Maximum Spatial Field Gradient	20-T/m (2,000-G/cm)
RF Excitation	Circularly Polarized (CP)
Operating Mode	Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg (Normal Operating Mode)
Scan Duration and Wait Time	Up to 60 minutes of scan duration
MR Image Artifact	In non-clinical testing, the image artifact caused by the device extends approximately 12mm from the AMDS Hybrid Prosthesis when imaged with a gradient echo pulse sequence and a 3.0-Tesla MR system. The lumen of this stent cannot be visualized on the gradient echo pulse sequence.

Patients who have other MR Conditional devices can be scanned as long as all the MR Conditional scan parameters for each of the devices are met. Do not conduct an MRI scan if any conditions for safe scanning for any device cannot be met. Nonclinical testing was performed using the thorax as the landmark position for MRI scanning; there are no exclusions. Under the scan conditions defined, an implant from the AMDS™ Hybrid Prosthesis is expected to produce a maximum temperature rise of 5°C after 15-minutes of continuous scanning (i.e., per pulse sequence).

8.0 PATIENT SELECTION AND TREATMENT

8.1 PATIENT SELECTION

Each patient should be evaluated by their physician to determine if hemiarch repair with the AMDS™ Hybrid Prosthesis is the most appropriate treatment for their acute DeBakey Type I aortic dissection. Consideration should be given to the individual patient condition, including age and life expectancy, comorbidities, patient tolerance for general anesthesia, cardiopulmonary bypass and hypothermic circulatory arrest, presence of secondary entry tears that may necessitate future procedures (e.g., a more extensive total arch repair with or without a frozen elephant trunk device), and the ability and willingness of the patient to complete the recommend clinical and imaging follow-up visits after the procedure.

8.2 DEVICE SIZING GUIDELINES

The aorta is sized based on a contrast enhanced CT scan or MR- Angiography of the chest using 2D and/or 3D imaging. Using the pre-op CT scan, measure the aortic vessel diameters (defined by adventitia-to-adventitia [outer wall to outer wall] measurements):

- D1: Measure the proximal diameter at the level between the innominate and left common carotid artery.
- D2: Measure the distal diameter at the level of the tracheal or pulmonary artery bifurcation to determine the tapered or straight configuration.

The operator can also estimate the ultimate length of the AMDS using ***Table 1*** **and** ***Figure 3*** to approximate distal landing zone.

8.3 PATIENT COUNSELING

The physician should counsel the patient on all associated risks and benefits of the AMDS™ Hybrid Prosthesis and its associated procedures, preferably in written form, including but not limited to:

- Patient age, risks, and benefits of the procedure with respect to the patient condition and comorbidities, and life expectancy
- Risks related to other treatment options (e.g., medical management, alternative surgical options, non-intervention)
- Safety and effectiveness of the AMDS™ Hybrid Prosthesis with the possibility of future reinterventions for disease progression
- Long-term follow-up and periodic imaging appointments needed to assess the status of the patients' health and device performance
- Symptoms of specific clinical sequelae (e.g., continued perfusion to the false lumen through secondary tears)

9.0 DEVICE STORAGE, RETURNS AND DISPOSAL

The AMDS, in its protective packaging, should be stored at room temperature, specifically not less than 0°C and not more than 25°C, and in a dry location. At the end of the procedure, care must be taken to ensure safe disposal of the AMDS delivery system. The surgical team should dispose of the AMDS delivery system in a biohazard waste disposal per hospital procedures.

Prior authorization from Artivion Customer Service is required for the return of any product. For any questions regarding AMDS or for return authorization, please contact Customer Service.

10.0 EQUIPMENT

- Surgical instruments for standard hemiarch repair
- Conventional ascending aorta polyester graft
- Sterile drape
- Sterile surgical sutures
- Standard PTFE Surgical Felt
- 0.035" stiff guidewire intended for cardiac procedures (Optional)

11.0 DIRECTIONS FOR USE – AMDS PROCEDURE

11.1 Preparation of the Aorta and Distal Anastomosis

The ascending aorta is transected and removed in a routine manner utilizing hypothermic circulatory arrest. The operator must ensure to leave at least 10 mm (1.0 cm) aortic tissue proximal to the native arch branch vessels that will be preserved in order to leave room for the 10mm PTFE felt portion of AMDS and avoid interruption of flow to the supra-aortic vessels. Initially the lesser curvature should be left longer to simplify the attachment of the AMDS to the aorta. The excess aortic tissue should be resected up to the level of the AMDS PTFE graft after the AMDS is secured to the aorta and prior to performing the anastomosis to the conventional graft. More than 1.0 cm of aortic tissue should be left in place proximal to the innominate artery or any of the arch branches that are intended to be preserved (***Figure 4***). Visually inspect the aorta to identify the true and false lumen prior to AMDS insertion.

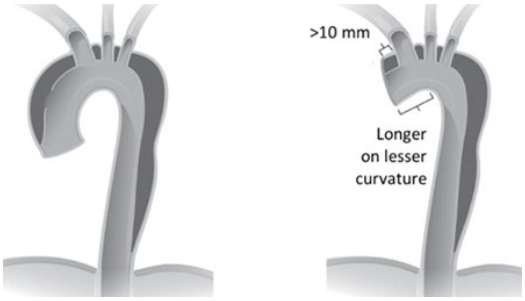

Figure 4. Preoperative intact ascending aorta (Left) and transected aortic prepared for the AMDS (Right)

11.2 AMDS System Preparation

Visually inspect the device packaging. If the package has been previously opened or the seal is damaged, discard and replace with a new package. Pre-soak the AMDS in saline. After soaking, flush the catheter with saline through the port using a 10mL sterile syringe until saline exits the pigtail tip.

WARNING: Do not remove the protective sheath until the device is advanced in the vessel. Premature removal of the protective sheath may result in device damage or early expansion, which may result in patient injury.

11.3 AMDS Insertion and Positioning

11.3.1 Insert the AMDS into the true lumen through the open distal aorta until the PTFE Felt Cuff is in the same plane; use of a stiff 0.035" guidewire (e.g. Lunderquist or alternative) is optional to ensure insertion into the true lumen. If a guidewire is used, it should be inserted via transfemoral approach prior to placing the patient on cardiopulmonary bypass (CPB) or while on CPB prior to inducing hypothermic arrest. Confirm guidewire position within the true lumen using TEE or IVUS.

11.3.2 Insert AMDS into the true lumen of the aorta until the cuff of the device is in the same plane as the transected distal aorta. The device is symmetrical and therefore does not require rotational orientation (***Figure 5***).

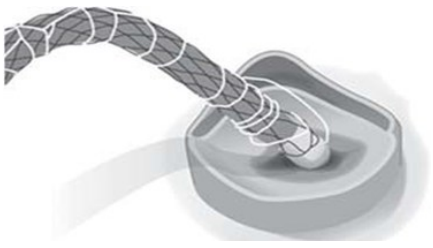

Figure 5. Insertion of the AMDS into transected aorta

CAUTION: Avoid twisting the system when inserting and deploying the stent to ensure complete expansion.

11.3.3 Following insertion of the delivery system into the aorta, confirm the AMDS stent is located in the true lumen prior to deployment.

CAUTION: Failure to deploy the stent in the true lumen may result in device malposition, persistent false lumen malperfusion or persistent malperfusion of the visceral organs, prolonged procedure time, and/or explant of the AMDS stent with or without a second AMDS implantation.

11.4 AMDS DEPLOYMENT

11.4.1 After the AMDS is positioned in the aorta and the edge of the AMDS collar is at the level of the transected edge of the aorta, retract the protective sheath to fully expose the cuff (see **Figure 6**). Remove the protective sheath and discard.

11.4.2 Stabilize the cuff by placing interrupted sutures to tack the cuff to the proximal-most inner aspect of the transected aorta (***Figure 7***). Use of a surgical PTFE felt strip external to the aorta is highly recommended to avoid excessive tension on or tearing of the aorta. Align the AMDS cuff with the adjacent section of the aorta and place 4 tacking sutures respectively approximately 90° apart. Repeat across the entire 360-degree circumference of the aorta. Once the AMDS cuff is tacked to the aorta, visually inspect the supra- aortic branches to ensure to avoid any inadvertent blockage of these vessels by the PTFE felt component

Figure 6. Position cuff at edge of transected aorta

Figure 7. Suture cuff to transected aorta

CAUTION: While placing the tacking sutures, use care to ensure that the tacking suture is not looped around the deployment suture as this may cause damage to the deployment suture.

11.4.3 If a guidewire was used, it should be removed prior to deployment of the AMDS stent. While an assistant stabilizes the AMDS cuff to the aorta using gentle vascular pickups, unscrew the green cap in a counterclockwise fashion to release the green cap in preparation to pull the deployment suture. Pulling the deployment suture will open the stent from a proximal to a distal direction on the delivery system. The operator should then:

- maintain grip of the AMDS handle to prevent rotation of the delivery system
- pull the deployment suture back until it is completely free of the delivery system and AMDS stent is fully deployed

CAUTION: Avoid forward pressure or rotation on the delivery system during deployment of the stent.

11.4.4 Following the deployment of the device (pulling of the green cap), ensure the entire deployment suture is removed, confirming that the device is in a fully deployed position. The minimum deployment suture length for each configuration is referenced in ***Table 1***.

CAUTION: If mis-deployment occurs (e.g., the stent is mal-positioned or fails to expand within the aorta), the implant may be carefully removed by cutting the tacking sutures (e.g., sutures previously placed to attach the cuff to the aorta) and slowly pulling the AMDS stent (with or without the delivery system) from the aorta. Withdrawal of the AMDS stent may lead to vascular damage.

11.4.5 Once the stent is released and disengaged from the delivery mechanism, remove the delivery system, making sure the tip of the delivery system is free from the distal end of the stent. If resistance is felt during delivery system removal after the AMDS is deployed, a guidewire may be placed through the delivery system to uncurl the tip to straighten the delivery system.

CAUTION: Do not forcefully pull on the delivery system after deployment of the AMDS, as the tip may be caught within the stent struts which may result in stent malposition or dislodgement.

CAUTION: Balloon dilatation of the AMDS stent is not recommended and should not be used to dilate the stent frame under normal use or in the event of limited stent expansion; balloon dilatation of the stent may lead to vascular trauma, stent migration, or aortic rupture.

11.5 ANASTOMOSES

11.5.1 Once the delivery system is removed, confirm successful deployment through visual inspection by looking within the aorta to see that the stent is fully deployed and then prepare the aortic anastomosis.

11.5.2 Completely secure the aortic layers by running a continuous suture layer circumferentially around the transected aorta, attaching the AMDS cuff through the aorta and to the external PTFE felt strip (see ***Figure 8A*** and ***Figure 8B***). There should be no folding of the inner felt as it may allow blood flow to find its way to the false lumen once flow is established. It may be helpful for an assistant to stretch the inner AMDS felt layer while completing the anastomosis.

11.5.3 Once this suture line is complete, any of the approved aortic replacement grafts may be chosen and the graft to aorta distal anastomosis performed in a conventional way. All dissected aortic tissue should be removed proximal to the AMDS. The anastomosis between the conventional polyester graft and the AMDS-aorta complex should be performed with each suture bite incorporating the conventional graft and the surgical felt-aorta- AMDS cuff complex creating a meticulously tight seal between the PTFE felts and the dissected aorta. This technique in essence allows the operator to anastomose the conventional graft to the AMDS "washer" created from surgical felt-aorta-AMDS cuff to create a sealed and secure anastomosis (***Figure 8C***). Routine intra-op and/or post-op imaging may be performed to confirm deployment and/or position of the device.

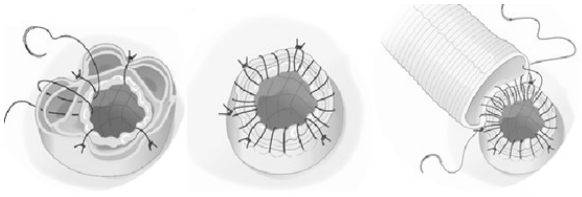

Figure 8. Complete the sequential anastomoses steps

CAUTION: The conventional aortic graft must be anastomosed to the aorta incorporating the conventional graft, aortic wall and the PTFE felt in each suture bite.

12.0 PATIENT FOLLOW-UP

All patients should undergo periodic imaging as advised by their physician. Patients experiencing reduced blood flow through the true lumen or dilation of the false lumen may need additional interventions.

No specific anti-platelet or anticoagulant therapy is recommended for patients who have received the AMDS device. Hence, postoperative anti-platelet or anticoagulant therapy should be instituted in accordance with standard practice following surgical repair of ATAD and at the discretion of the treating medical team.

13. SUMMARY OF PRIMARY CLINCAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for treatment of patients with Acute DeBakey I dissections with the AMDS as an adjunct to conventional surgery (e.g., ascending/hemiarch repair) in the US under IDE #G210218. Data from the PERSEVERE Pivotal IDE were the basis for the PMA Approval Decision. Additional foreign studies, including the DARTS I Study and Berlin Heart Study, were used to support the PMA as additional supplementary clinical data.

13.1. Study Design (PERSEVERE)

Patients were treated between 17-Jul-2022 and 6-Nov-2023. The database for this PMA reflected data collected through 12-Jan-2026 and included 93 subjects. There were 26 US investigational sites. The PERSEVERE Study is a prospective, single-arm, multi-center pivotal IDE study of the AMDS for treatment of patients with Acute DeBakey I dissections with clinical or radiographic malperfusion. Patients were consented pre-operatively and were considered enrolled only after AMDS implantation. The intended study follow-up period is 5 years after AMDS surgery. The data includes complete, 1-year adjudicated follow-up data of 63 subjects; additional longer term data is also available.

The PERSEVERE study has two co-primary endpoints to establish safety and effectiveness which are defined below:

- Patients experiencing at least one of the following major adverse events (MAEs) occurring ≤30-days post-procedure: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, and myocardial infarction. The results were tested against a performance goal of 58% which was derived as the average rate of patients with ≥1 MAE estimated from 5 publications reporting outcomes following the standard of care (hemiarch procedure)[1]. Sample size was calculated assuming enrollment of 84 patients with an expected drop-out rate of 10% at 30-days, which would require 93 patients to achieve the statistical assumptions under an assumed true AMDS 30-day MAE rate of 40%.
- Patients with Distal Anastomotic New Entry (DANE) tears documented by the independent Core Lab on a post-operative CTA ≤30 days post-procedure. The results were tested against a performance goal of 45% which was derived as the weighted average rate of patients with DANE from 4 publications reporting outcomes following the standard of care (hemiarch procedure)[2]. Sample size was calculated assuming a minimum of 17 patients with an expected drop-out rate of 10% at 30-days, which would require 19 patients to achieve the statistical assumptions under an assumed true AMDS 30-day MAE rate of 10%. Considering both primary endpoints, the larger sample size of 93 patients was planned for this study.

Evaluation of the 30-day PERSEVERE data supported the HDE approval. At the time of PMA approval, complete, adjudicated 1-year follow-up data for all evaluable PERSEVERE study subjects was provided, as well as available longer-term information.

For each co-primary endpoint, a one-sided exact binomial test will be used to construct the 95% exact (Clopper-Pearson) confidence interval ($\alpha = 0.025$).

External evaluation groups used during the PERSEVERE study included:

- An imaging Core Laboratory was used to perform independent assessments of computed tomography (CT)/computed tomography with angiography (CTA), X-Ray and duplex ultrasound (DUS) imaging submitted by clinical sites. The Core Laboratory assessments were used for all radiographic analyses.
- An external Clinical Events Committee (CEC) adjudicated the primary endpoint major adverse events (MAEs) and select adverse events.

13.1.1 Clinical Inclusion and Exclusion Criteria

Enrollment in the PERSEVERE study was limited to patients who met the following inclusion criteria: ≥18 years of age or ≤80 years of age at time of surgery, with acute DeBakey type I dissection based on computed tomography angiography (CTA) and diagnosed ≤14 days from of the index event, with the presence of malperfusion (cerebral, visceral, renal, spinal cord, and/or peripheral).

Patients were not permitted to enroll in the PERSEVERE study if they met any of the following key exclusion criteria (this is not a comprehensive list):

- A primary entry tear that extends into the aortic arch or distal to the left subclavian artery
- Need for a total aortic arch replacement and/or repair or reconstruction of any part of the arch and branch vessels (including extra-anatomic bypass of the branch vessels), for any reason, as deemed necessary by the Investigator
- Aortic fistulous communication with non-vascular structure (e.g., esophagus, bronchial)
- Extensive thrombus or calcifications in the aortic arch as defined by CTA
- Excessive tortuosity precluding safe passage of AMDS as defined by CTA
- Descending thoracic aneurysm involving the proximal third (one-third) of the descending aorta and measuring >45 mm in diameter
- Aortic arch aneurysm >50 mm in diameter
- Coronary malperfusion
- In circulatory shock (i.e., systolic blood pressure <90 mmHg) at time of screening
- In extreme hemodynamic compromise requiring cardiopulmonary resuscitation at time of screening
- Suspicion of bowel necrosis (as determined by the implanting physician based on imaging observations, peritoneal signs, surgical exploration, elevated serum lactate levels, low pH, and/or acidosis)
- Clinical or radiographic signs of bowel infarction or gastrointestinal hemorrhage
- Base deficit > -10 mmol/L or -10 mEq/L

[1] Bossone E, R. V., Nienaber CA, Trimarchi S, Ballotta A, Cooper JV, Smith DE, Eagle KA, Mehta RH. (2002). Usefulness of Pulse Deficit to Predict In-Hospital Complications and Mortality in Patients With Acute Type A Aortic Dissection. Am J Cardiol, 89, 851-855;
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Girdauskas E, K. T., Borger MA, Falk V, Mohr FW. (2009). Surgical risk of preoperative malperfusion in acute type A aortic dissection. J Thorac Cardiovasc Surg, 138, 1363-1369;
Pacini D, L. A., Belotti LM, Fortuna D, Gabbieri D, Zussa C, Contini A, Di Bartolomeo R, et al. . (2013). Acute type A aortic dissection: significance of multiorgan malperfusion. Eur J Cardiothorac Surg, 43, 820-826;
Zindovic I, G. T., Ahlsson A, Fuglsang S, Gunn J, Hansson EC, Hjortdal V, Jarvela K, Jeppsson A, et al. . (2019). Malperfusion in acute type A aortic dissection: an update from the Nordic Consortium for Acute Type A Aortic Dissection. J Thorac Cardiovasc Surg. , 157, 1324-1333.
[2] Bing, F., Rodiere, M., Martinelli, T., Monnin-Bares, V., Chavanon, O., Bach, V., & al., e. (2014). Type A Acute Aortic Dissection Why Does the False Channel Remain Patent After Surgery. Vasc Endovasc Surg, 48(3), 239-245;
Ergin MA, P. R., Galla JD, Lansman SL, Mendelson DS, Quintana CS, Griepp RB. (1994). Significance of distal false lumen after type A dissection repair. Ann Thorac Surg, 57, 820-824;
Rylski B, H. N., Beyersdorf F, Kondov S, Wolkewitz M, Blanke P, Plonek T, Czerny M, Siepe M. (2017). Fate of the dissected aortic arch after ascending replacement in type A aortic dissection. Eur J Cardiothorac Surg, 51, 1127-1134;
Tamura K, C. G., Hiraoka A, Totsugawa T, Sakaguchi T, Yoshitaka H. (2017). The progsnostic impact of distal anastomotic new entry after acute type I aortic dissection repair. Eur J Cardiothorac Su(52), 867-873.

- Previous placement of a thoracic endovascular graft
- Interventional and/or open surgical procedures 30 days prior to the dissection repair
- Planned major interventional and/or open surgical procedures 30 days post the dissection repair
- Previously diagnosed with Marfan syndrome, Ehlers-Danlos syndrome, or Loeys-Dietz syndrome based on laboratory genetic testing
- Diagnosed with acute myocardial infarction in the 30 days prior to the dissection diagnosis
- Diagnosed with severe and catastrophic neurological complications in the 30 days prior to the dissection diagnosis (i.e., obtundation or coma)
- Current Stage 5 End stage chronic kidney disease (estimated Glomerular Filtration Rate [eGFR] ≤15 mL/min)

13.1.2 Follow-up Schedule

All patients were scheduled to return for follow-up examinations at discharge/30-days (+/- 14 days), 3-6-months (+/- 7 days), 12-months (+/- 8 weeks), and annually through 5-years (+/- 12 weeks). The assessments performed at each visit are listed in ***Table 2***. Adverse events were recorded at all visits.

Table 2. PERSEVERE Study Visit Schedule of Assessments

PROTOCOL ACTIVITY	Visit 1	Visit 2		Visit 3	Visit 4	Visit 5	Visits 6-9
	Pre-Op	Procedure	Discharge	30-days[1]	3-6 months	1 year	2- 5 years
	≤14 days from procedure	<24 hrs post-op	≥24 hrs post-op	+/-14 days	+/-7 days	+/- 8 wks	+/- 12 wks
Informed Consent, Eligibility and Baseline Assessments	X						
Concomitant Medication and Patient Exam	X		X	X	X	X	X
Blood tests	X	X	X	X	X	X	X
CT /CTA Imaging Evaluation (chest/ abdomen & pelvis)	X			X	X	X	X
Brain Imaging (CT and/ or MRI) and NIHSS in patients with stroke per site procedure	*	*	*	*	*	*	*
Electrocardiogram (ECG)			X				
mRS	X		X		*	*	*
Procedure & Device Sizing and Technical Success		X					
Adverse Events and additional Post-Op Procedures		X	X	X	X	X	X
Quality of Life Assessment (SF-12v2)			X	X	X	X	X
Procedural /Treatment Success				X	X	X	X

X=Study Specific Activity [includes data collection only]
[1] If the patient's hospital discharge was ≥14 days after surgery, then data collected at discharge was not recollected for Visit 3 unless discharge occurred prior to 30-day window and new protocol-specified information is available (ex. any SAE incidence) within the Visit 3 window.
* Need is determined by site's standard of care or as event occurs
Abbreviations: mRS =modified Rankin Score; NIHSS = National Institutes of Health Stroke Scale; Pre-op = preoperative; Post-op= post-operative, wks = weeks; hrs=hours; SF-12 = 12-item Short Form Survey

13.1.3 Clinical Endpoints

The co-primary endpoints include the following:

Patients experiencing at least one of the following major adverse events (MAEs) occurring ≤30-days post-procedure: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, myocardial infarction. The co-primary endpoint was compared to a performance goal of 58%.

Patients with DANE tears documented by the independent Core Lab on a post-operative CTA ≤30-days post-procedure. The co-primary endpoint was compared to a performance goal of 45%.

The performance goals are based on literature reported rates of MAEs[3] and DANE[4] in malperfusion patients with the surgical procedure (without AMDS).

The PERSEVERE pivotal study primary endpoint analysis supported the HDE. Additional longer-term data supported the PMA.

The secondary safety endpoints included are assessed at all post-discharge visits:

- Analysis of rates of MAEs, mortality, additional aortic procedures, device related events, false lumen response, and supra-aortic branch vessel patency. Additional major adverse events included in the secondary endpoint analysis are listed below:

  - Aortic rupture
  - Bowel ischemia
  - Hypersensitivity
  - Myocardial infarction
  - New disabling and non-disabling stroke
  - New postoperative paraplegia/paraparesis
  - New postoperative organ malperfusion, including cerebral, coronary, visceral, renal, spinal cord, and peripheral
  - New onset renal failure requiring dialysis
  - Pseudoaneurysm

[3] Zindovic et al., "Malperfusion in Acute Type A Aortic Dissection."; Pacini et al., "Significance of Multiorgan Malperfusion."; Girdauskas et al., "Surgical Risk of Preoperative Malperfusion in Acute Type A Aortic Dissection."; Geirsson et al., "Significance of Malperfusion Syndromes Prior to Contemporary Surgical Repair for Acute Type A Dissection."; Bossone et al., "Usefulness of Pulse Deficit to Predict In-Hospital Complications and Mortality in Patients with Acute Type A Aortic Dissection."
[4] Bing et al., "Type A Acute Aortic Dissection: Why Does the False Channel Remain Patent After Surgery."; Ergin et al., "Significance of Distal False Lumen After Type A Dissection Repair."; Rylski et al., "Fate of the Dissected Aortic Arch After Ascending Replacement in Type A Aortic Dissection."; Tamura et al., "Prognostic Impact of Distal Anastomotic New Entry After Acute Type I Aortic Dissection Repair."

- Recurrent laryngeal or phrenic nerve injury
- Respiratory failure (need for reintubation or ventilator dependence >48 hours)
- Severe heart failure requiring mechanical circulatory support
- Thromboembolic adverse events

Additional effectiveness endpoints included:

- Remodeling outcomes (measurement and change in total aortic diameter, true lumen diameter, false lumen diameter, clinically meaningful (≥ 6.0mm) true lumen expansion, and false lumen response were summarized descriptively at each post-discharge visits.

The secondary composite endpoints included technical and procedural success rates as defined below:

- Technical Success at conclusion of the index procedure: Successful delivery and accurate placement of the device at the intended implantation site and retrieval of the device delivery system, patency of the device and aortic arch vessels at the conclusion of the procedure, and no need for unanticipated or emergency surgery to correct a device malfunction or reintervention due to device-related complications.
- Procedural Success at 30-days post-procedure: Technical success with the absence of the following: death, major adverse ischemic events, including new disabling stroke (modified Rankin Score [mRS] > 2 with change from baseline > 1), new postoperative paraplegia or paraparesis, new ischemia due to branch vessel compromise related to the procedure, distal procedure-related thromboembolic events, and any additional unplanned surgical or interventional procedures related to the device since completion of the original procedure.

13.1.4 Accountability of PMA Cohort

At the time of database lock, of 93 subjects enrolled in the PMA study, 63 subjects (67.7%) are available for analysis at 1-year.

The primary analysis population includes all patients who were enrolled, treated with the AMDS device, and had evaluable data for the co-primary endpoints. The Safety population (SP) includes all patients treated with the AMDS device. Analyses in this document are based on the Safety population.

Patient follow-up, imaging quality, and patient status at each follow-up time point is shown in ***Table 3***.

Table 3. Follow-Up Compliance and Imaging Quality Summary[5]

Visit Details			Subjects with Data for Visit and Subject Status					Imaging Compliance and Quality to Assess Parameters of Interest[4]		
Visit #	Visit Description[1]	Eligible for follow-up[2]	Subjects with Data for Visit[8]	Subjects with Missed Visit	Death	LTF/ Withdrawn	Not due for next visit[3]	CT/CTA read by Core Lab	TL Diameter at Zone 3	DANE
		#	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)
1	Pre-Op	93	93(100.0%)	NA	NA	NA	0(0.0%)	93(100.0%)[5]	91(97.8%)[5]	NA
2	Procedure through Discharge	93	93(100.0%)	NA	NA	NA	0(0.0%)	57(61.3%)	49(52.7%)	44(47.3%)
3	30-days (+/- 14 days)	93	79(84.9%)[7]	5(5.4%)[8]	9(9.7%)[7]	0(0.0%)	0(0.0%)	69(82.1%)[6]	64(76.2%)[6]	62(73.8%)[6]
4	31-180 days	84	71(84.5%)	9(10.7%)	4(4.8%)	0(0.0%)	0(0.0%)	69(86.3%)	66(82.5%)	65(81.3%)
5	181-365 days	80	63(78.8%)	7(8.8%)	6(7.5%)	4(5.0%)	0(0.0%)	56(80.0%)	53(75.7%)	54(77.1%)
6	366-730 days	70	48(68.6%)	11(15.7%)	4(5.7%)	7(10.0%)	34	41(65.1%)	39(61.9%)	38(60.3%)

[1]Some of the time periods reflect the time between scheduled visits; however, some visits may have deviated from the listed period due to compliance issues.
[2]Eligible for follow-up = eligible for follow-up from the previous interval – [death+LTF+not due for next visit].
[3]Those subjects that are "Not due for next visit" are those subjects that are not within the follow-up window for the next interval.
[4]The data represents the existence of available data, and these numbers do not reflect incidence of reported events.
[5]Two additional pre-operative CTAs were retrieved and assessed after the HDE analysis; data here reflects the additional data.
[6]One additional 30-day CTA was assessed after the HDE analysis due to delays in obtaining the CTA; data here reflects the additional data.
[7]After the HDE analysis, 1 additional 30-day visit occurred.
[8]There are no pending visits through 2 years at the time of data export.
Note: There are changes from data presented in the HDE due to minor reorganization of data presentation.

Abbreviations: EFU=Eligible for Follow-up, NA=Not applicable, CT=computed tomography, CTA=computed tomography angiography, TL=true lumen, LTF=lost-to-follow-up, DANE= distal anastomotic new entry

13.1.5 Study Population Demographics and Baseline Parameters

Demographics and Baseline Characteristics

The demographics of the study population are typical for an acute DeBakey Type I Dissection study performed in the US.

A total of 93 patients with acute DeBakey Type I dissection were enrolled in PERSEVERE. Patients were mostly male (78.5%) with a mean age of 58.7 ± 9.52 years. All patients presented with preoperative clinical (81.7%) or radiographic (18.3%) malperfusion in at least one organ system. Comorbidities most commonly included history of arterial hypertension (37.6%), chronic kidney disease (35.5%), cardiac arrhythmia (20.4%), diabetes (15.1%), coronary artery disease (CAD) (11.8%), cancer (11.8%), and chronic pulmonary obstructive disease (COPD) (10.8%) (see ***Table 4).***

Table 4. Patient Baseline Characteristics (PERSEVERE)

Characteristics	Total Patients (n=93)[4]
Demographics and Baseline Characteristics	
Age (years)[1]	58.7 ± 9.52
Male	78.5%
Preoperative Clinical Malperfusion[1]	76 (81.7%)
Preoperative Radiographic Malperfusion Only[1]	17 (18.3%)
Race	
Asian	1 (1.1%)
Black or African American[1]	21 (22.6%)
White	56 (60.2%)
Other[1]	2 (2.2%)
Unknown or missing[1]	13 (14.0%)
Ethnicity	
Non-Hispanic[1]	75 (80.6%)
Hispanic[2]	10 (10.8%)
Unknown[1]	8 (8.6%)
	# (%) (n=93)
Aortic Arch Anatomy *(>1 anatomy may be applicable to 1 patient)*	
Normal (3 great vessels) [1]	67 (72.0%)
Bovine Arch[1]	22 (23.7%)
Isolated Vertebral[1]	5 (5.4%)
Not documented/assessed[1]	1 (1.1%)
Primary entry tear in Zone 0 documented by Core Lab[1]	87 (93.5%)
Primary entry tear beyond Zone 0 documented by Core Lab[1]	3 (3.2%)
Primary entry tear data missing[1]	3 (3.2%)
Medical History	**# (%) (n=93)**
Cardiac Arrhythmia[3]	19 (20.4%)
Congestive Heart Failure (CHF) [3]	4 (4.3%)
Coronary Artery Disease (CAD) [3]	11 (11.8%)
Chronic Pulmonary Obstructive Disease (COPD) [3]	10 (10.8%)
Peripheral Arterial Disease[3]	0 (0%)
Hypertension (stage 1 and above) [2]	35 (37.6%)
Liver Disease	5 (5.4%)
Cancer	11 (11.8%)
Chronic Kidney Disease[2]	33 (35.5%)
Diabetes (Type I or II) [2]	14 (15.1%)
Prior Stroke	5 (5.4%)
Prior TIA	5 (5.4%)
Prior Myocardial Infarction	3 (3.2%)
Prior Thromboembolic Event (DVT)	4 (4.3%)
Prior CABG[3]	0 (0%)
Prior PCI	5 (5.4%)
Previous Cardiac Intervention – Other	4 (4.3%)

[1]This value has been updated from that presented for the HDE to address data entry errors.
[2]The field description has been altered from the HDE for clarification.
[3]Formatting of the value has been updated from that presented in the HDE for consistency.
[4] One patient was identified to have end stage renal disease after HDE approval. This is one of the study's exclusion criteria and the data presented in this table and below contains data including the patient despite the major protocol deviation.

Procedural Characteristics

Hemiarch repair was performed in 100% of patients, with concomitant procedures performed in 85% of patients. The duration for the total procedure and AMDS implantation is shown in ***Table 5***.

Table 5. Procedural Characteristics (PERSEVERE)

Procedural Characteristics		**% Patients**
Concomitant Procedures	None (Hemiarch + AMDS only)[1]	14 (15.1%)
	Aortic Valve Resuspension[2]	35 (37.6%)
	Aortic Root Repair or Replacement[1]	37 (39.8%)
	Aortic Valve Repair or Replacement[1]	22 (23.7%)
	Coronary Artery Bypass Surgery (CABG)	5 (5.4%)
	Other[1]	23 (24.7%)
		Median (Range)
Procedure Times	AMDS Deployment Time (min)[3]	4 (0-11)
	Cardiopulmonary Bypass (CPB) Duration Time (min) [1]	176.0 (91-403)
	Hypothermic Circulatory Arrest (min)	28 (0-168)
	Cerebral Perfusion Time (min)	28 (10-230)
	Total AMDS Implantation Time (min)[4]	15 (5-32)

[1]This value has been updated from that presented for the HDE to address data entry errors.
[2]This value has been added from that presented for the HDE to address data completeness.
[3]Defined as time from AMDS delivery system insertion to delivery system removal.
[4]Defined as time from AMDS Delivery system insertion to completion of AMDS to aorta anastomosis.

13.1.6 Safety and Effectiveness Results

1. Co-Primary Endpoints

The analysis of the co-primary endpoints was based on the available data through 30-days follow-up visit for all 93 subjects. Complete, adjudicated data included in the co-primary endpoint for major adverse events (MAE) occurring within 30 days post-procedure are shown in ***Table 6***.

A total of 78/93 (85%) patients had a CTA which confirmed absence of DANE prior to (during the pre-discharge CTA assessment) or during 30-day follow-up. Therefore, 15 patients had an unknown DANE status through 30-days.

The imaging Core Lab reported no subjects with DANE (95% CI: 0%, 3.9%) compared to the performance goal of 45%. Patients experiencing at least one of the MAEs was 26.9% (95% CI: 18.4%, 37.4%) compared to the performance goal of 58%. The co-primary endpoints were met based upon the data through 30-days.

Sensitivity Analysis

Considering the worst-case scenario for missing DANE data, a DANE rate of 15/93 (16.1%) [95% CI: 9.32, 25.2] was calculated and an exact binomial test with one-sided p-value still revealed a statistically significant difference between the worst-case DANE rate and the performance goal ($p<0.001$).

Table 6. Primary Endpoint Events through 30-Days (PERSEVERE)

	Total Number of Patients ≥1 CEC Adjudicated Event # (%), n=93
All-cause Mortality	9 (9.7%)
New Disabling Stroke[1]	10 (10.8%)
New Onset Renal Failure Requiring Dialysis	18 (19.4%)
Myocardial Infarction	0 (0%)
Co-Primary Endpoint: Total # of Patients with ≥ 1 MAE[1, 2]	25 (26.9%) (95% CI: 18.4, 37.4)
	Total Number of Patients Core Lab Reported #(%) n=78[3]
Co-Primary Endpoint: # of Patients with Distal Anastomotic New Entry (DANE) Tear	0 (0%) (95% CI: 0%, 3.9%)

[1] This value has been updated from that presented for the HDE to address a data entry error; a subject's pre-operative mRS score was re-evaluated after contradicting information on pre-operative stroke was discovered.
[2]Of the 38 MAEs (1 patient had 2 strokes) in 25 patients, 17 were adjudicated by the CEC as at least possibly device related and 36 were adjudicated by the CEC as at least procedure related.
[3]The denominator has been updated from that presented in the HDE to reflect the totality of subjects with CT data available pre-discharge or at the 30-day visit.
Definition: New disabling stroke (defined as a change in the modified Rankin Score (mRS) > 2, with a change from baseline >1).

2. Secondary Endpoints

Secondary endpoints included secondary safety endpoint analysis, technical success and procedural success, and aortic remodeling in the treated segment.

Safety Events through 2-Year Available Follow-Up

The following safety events were observed at any point through 2-year follow-up:

- all-cause death (23/93, 24.7%)

- CEC Adjudicated: At least Possibly Device Related 4/23; At least Possibly Procedure Related 9/23
- new disabling stroke (11/93, 11.8%)
  - 13 events occurred in 11 patients. CEC Adjudicated: At least Possibly Device Related 13/13, At least Possibly Procedure Related 11/13
- new non-disabling stroke (6/93, 6.5%)
  - 7 events occurred in 6 patients. CEC Adjudicated: At least Possibly Device Related 7/7, At least Possibly Procedure Related 3/7
- new onset of renal failure requiring dialysis (19/93, 20.4%)
  - CEC Adjudicated: At least Possibly Device Related 3/19, At least Possibly Procedure Related 17/19
- myocardial infarction (2/93, 2.2%)
  - CEC Adjudicated: At least Possibly Device Related 0/2, At least Possibly Procedure Related 2/2
- respiratory failure (18/93, 19.4%)
- thromboembolic events (8/93, 8.6%)
- new post-operative organ malperfusion (4/93, 4.3%)
- pseudoaneurysm (3/93, 3.2%)
  - CEC Adjudicated: At least Possibly Device Related 2/3, At least Possibly Procedure Related 3/3
- bowel ischemia (2/93, 2.2%)
  - CEC Adjudicated: At least Possibly Device Related 0/2, At least Possibly Procedure Related 1/2

. Aortic rupture, hypersensitivity, new post-operative paraplegia or paraparesis, recurrent laryngeal or phrenic nerve injury, and severe heart failure requiring mechanical circulatory support were not observed. Through 2-years, 10 patients required 15 additional aortic procedures, including intervention on any segment of the aorta or main aortic branches. Procedures were performed open (9) or either endovascular or percutaneous (6) and indicated for aortic aneurysm growth (7), pseudoaneurysm (4), lower limb ischemia (1), aortic thrombus (1), right common carotid artery stenosis (1), and endocarditis (1). There were no unanticipated device-related reoperations or complete explants; 1 partial explant was required after 1-year during an open thoracoabdominal repair.

Technical and Procedural Success

Technical success (delivery, deployment, catheter retrieval, AMDS and aortic arch vessel patency, freedom from device-related malfunction or reintervention) was reported in 98.9% of patients (n=92); in one patient the AMDS stent was inadvertently implanted in the false lumen through a distal secondary entry tear false lumen with no injury or clinical sequelae.

Procedural success was achieved in 75 of 93 patients (80.6%). The value has changed since data presented for the HDE due to data entry errors and the collection of new information. Eighteen patients did not achieve procedural success for one or more reasons. Categorization is summarized by the most significant reason for each patient and include the following reasons: 9 patients died, 8 patients had new disabling stroke (including one patient who failed technical success), and 1 patient who had new ischemia due to branch vessel complication. There were no cases of new paraplegia or paraparesis.

Device Related Events through Available Follow-up (Core Lab)

Considering all CTAs evaluated by the imaging Core Lab, there was no radiographic evidence of DANE, device migration, stent fracture, kink, or twist. D-SINE was observed in 2 patients and stent narrowing was identified by the Core Lab in 5 patients through all available follow-up; there are no reports of clinical sequelae associated with the occurrence of stent narrowing and d-SINE.

Aortic Remodeling and Patency through Available Follow-Up (Core Lab)

The aorta was analyzed at zones 1-3 to evaluate the change in maximal total aortic diameter, true lumen and false lumen diameter (***Table 7***), as well as false lumen status (***Table 8***). Aortic zones were defined by the Society of Thoracic Surgeons (STS)/Society of Vascular Surgeons (SVS) Aortic Zone Classification (see ***Figure 9***). The number of scans for each endpoint at each timepoint varied due to CTA quality issues, as well as anatomical and implant variations.

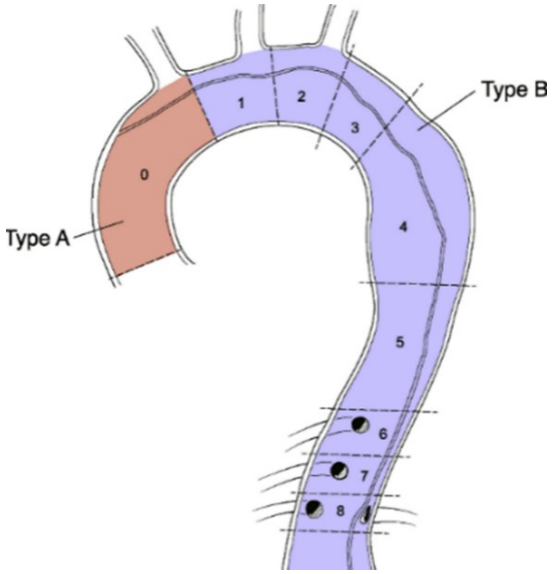


Figure 9. STS/SVS Aortic Zone Classification

Table 7. Aortic Remodeling – Diameter Change From Baseline (Pre-Procedure) Through Available Follow-Up [Mean (SD)] (Core Lab)

Aortic Zone	Total Aortic Diameter (mm)			True Lumen Diameter (mm)			False Lumen Diameter (mm)		
	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)
Zone 1	0.35 (3.409)	1.30 (3.680)	2.62 (3.537)	12.33 (4.954)	13.96 (4.897)	14.88 (6.380)	-12.01 (5.310)	-12.66 (5.317)	12.26 (5.926)
Zone 2	1.34 (3.607)	2.78 (3.900)	4.36 (3.847)	12.21 (4.972)	13.26 (4.998)	14.83 (5.886)	-10.90 (5.644)	-10.41 (6.159)	-10.31 (6.957)
Zone 3	3.15 (3.412)	5.85 (6.238)	8.71 (6.880)	6.87 (5.457)	7.64 (5.397)	8.36 (5.659)	-3.63 (6.210)	-1.88 (8.646)	0.35 (9.209)
Zone 4	4.10 (3.573)	7.84 (5.671)	10.34 (6.901)	7.94 (6.363)	7.70 (5.628)	8.90 (5.831)	-3.79 (6.997)	0.20 (8.330)	1.44 (9.103)
Zone 5	3.28 (1.962)	6.26 (3.687)	8.55 (4.178)	11.79 (7.640)	10.89 (7.925)	10.61 (9.210)	-8.48 (7.762)	-4.67 (8.530)	2.06 (10.711)

[1] Two additional baseline CTAs were retrieved and assessed after the analysis for HDE; this table reflects the additional data.

Table 8. Aortic Remodeling – False Lumen Thrombosis Status Through Available Follow-Up [n (%)] (Core Lab)

Aortic Zone	30-Days (n=69)[1,2]				1-Year (n=56)[1]				2-Years (N=41)[1]			
	CT	PT	PAT	NA	CT	PT	PAT	NA	CT	PT	PAT	NA
Zone 1	12 (15.2%)	29 (36.7%)	10 (12.7%)	21 (26.6%)	15 (23.8%)	27 (42.9%)	4 (6.3%)	10 (15.9%)	8 (17.4%)	14 (30.4%)	3 (6.5%)	14 (30.4%)
Zone 2	8 (10.1%)	41 (51.9%)	12 (15.2%)	11 (13.9%)	14 (22.2%)	35 (55.6%)	4 (6.3%)	3 (4.8%)	8 (17.4%)	23 (50.0%)	6 (13.0%)	2 (4.3%)
Zone 3	5 (6.3%)	46 (58.2%)	9 (11.4%)	12 (15.2%)	8 (12.7%)	38 (60.3%)	6 (9.5%)	4 (6.3%)	6 (13.0%)	29 (63.0%)	3 (6.5%)	1 (2.2%)
Zone 4	1 (1.3%)	50 (63.3%)	9 (11.4%)	12 (15.2%)	4 (6.3%)	44 (69.8%)	4 (6.3%)	4 (6.3%)	3 (6.5%)	31 (67.4%)	4 (8.7%)	1 (2.2%)
Zone 5	1 (1.3%)	45 (57.0%)	13 (16.5%)	13 (16.5%)	3 (4.8%)	44 (69.8%)	6 (9.5%)	3 (4.8%)	3 (6.5%)	31 (67.4%)	4 (8.7%)	1 (2.2%)

[1]Missing data is excluded in the table, which includes 7 (8.9%) patients at 30-days, 7 (11.1%) patients at 1-year, and 7 (15.2%) patients at 2-years
[2] Two additional baseline CTAs were retrieved and assessed after the HDE analysis; this table reflects the additional data.
Abbreviations: CT: Completely thrombosed, PT: Partially thrombosed, PAT: Patent, NA: Not assessed

Supra-aortic branch vessel patency was evaluated through 2-years. At 30-days, 1-year, and 2-year the innominate artery (IA) patency was, 95.2% (59/62), 96.2% (52/54), and 92.3% (36/39) respectively. The left common carotid patency was 95.2% (59/62), 98.1% (53/54), and 92.3% (36/39) at 30-day, 1-year and 2-year respectively. The Left Subclavian Artery patency was 96.8% (60/62), 100% (54/54) and 97.4% (38/39) at 30-days, 1-year and 2-year respectively. There were no artery occlusions in the Innominate artery (IA). Both occlusions that occurred were due to intentional surgical interventions.

3. Subgroup Analyses

The following preoperative characteristics were each evaluated for potential association with outcomes: age (<65 or ≥65 years old), female/male, BMI (<28 kg/m^2 or ≥28 kg/m^2), and radiographic/clinical pre-operative malperfusion. No correlations were found between the respective preoperative characteristics and study outcomes.

4. Pediatric Extrapolation

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

13.2. Summary of Supplemental Clinical Information

There is additional experience with the AMDS device outside of the United States (US). Key studies conducted outside of the US are briefly summarized below.

13.2.1 DARTS I

The DARTS I Study is a prospective, single-arm, multi-center study of AMDS in patients with Acute DeBakey I dissections. DARTS I enrolled 46 eligible subjects at 5 sites in Canada (n=39) and 1 site in Germany (n=7) from March 2017 to January 2019. Subjects were followed for 5-years. An independent imaging core laboratory evaluated the imaging obtained during the study. The study did not include a Clinical Events Committee nor a Data Safety Monitoring Board. DARTS I and PERSEVERE enrolled similar patient populations with the key difference being DARTS I enrolled subjects with both preoperative malperfusion (25/46) and non-malperfusion (21/46) and PERSEVERE included only patients with preoperative malperfusion. At 30-days, 31/38 (81.6%) of subjects had data for visit and 29/31 (76.3%) had CT/CTA data read by Core Lab. At 1-year, 35/36 (97.2%) of subjects had data for visit and 34/35 (97.1%) had CT/CTA data read by the Core Lab. At 3-years, 33/33 (100%) of subjects had data for the visit and 30/33 (90.9%) had CT/CTA read by the Core Lab. At 5-years, 27/27 (100%) of subjects had data for the visit and 25/27 (92.6%) had CT/CTA read by the Core Lab.

Key outcomes are summarized. Successful device deployment was reported in 43/46 subjects (93.5%) and 3/46 (6.5%) subjects had missing data. There were 12/46 (26%) deaths total at 5-years. There were 7 deaths ≤ 30-days from the procedure none were attributed by the sites as related to the procedure or device. There were 5/46 (10.8%) additional deaths beyond thirty days, of which one was considered by the investigator to be possibly related to the procedure and the device. A total of 11/46 subjects (23.9%) experienced neurological complications (all strokes) within the first 30 days, including 8/46 subjects (17.4%) who had new stroke (defined as a new disabling or non-disabling stroke in a subject absent of prior stroke or stroke symptoms pre-procedure). After 30-days, two additional subjects had a stroke making the total number of subjects with a stroke 10/46 (21.7%). In total, 4/46 subjects (8.7%) had evidence of device narrowing on ≥ 1 follow-up CTA; 1/46 subject (2.2%) had a device twist noted, along with narrowing. The core lab defined narrowing as a 50% reduction in device diameter in comparison to diameters directly proximal or distal to the measurement area. In all cases of narrowing, there was no clinical sequelae. There were no device fractures, device kinks, DANE or d-SINE noted by the Core Lab through 5-years. Complete or partial false lumen thrombosis was observed in 58-74% of subjects in Zone 1, 59-74% in Zone 2, and 65-83% in Zone 3 at pre-discharge through 5-years, with an increase observed over time.

The secondary endpoints also provide evidence of positive aortic remodeling, including total aortic diameter (TAD) stability, TL expansion, and FL reduction through 5-years in the treated aortic zones (1-3). Average TAD change from baseline was ≤2.1 mm in Zone 1, ≤2.7 mm in Zone 2, and ≤6.8 mm in Zone 3

through 5 years. Average TL expansion was ≥13.4 mm in Zone 1, ≥12 mm in Zone 2, and ≥7.3 mm in Zone 3 through 5 years, with an increase in expansion documented between pre-discharge and 5 years. Average FL reduction was ≥11.3 mm in Zone 1, ≥9.4 mm in Zone 2, and 0.6 mm in Zone 3 through 5-years; at 5-years, FL reduction was sustained in Zone 1, there was less reduction in Zone 2, and there was loss of reduction in Zone 3 compared to pre-discharge.

13.2.2 Berlin

The Berlin Heart Study published by Montagner et al.[5] provides real-world evidence of the commercial use of the AMDS in Europe. The AMDS was implanted in a total of 100 patients with acute DeBakey type I dissection at the Berlin Heart Center between February 2018 and June 2021. Patient baseline demographics illustrate the severity of the disease, with 35% of the cohort having acute neurological deficit and 46% with malperfusion; the remaining 54% of patients did not have malperfusion. Standard implantation technique was used, with moderate hypothermia at 28°C and 80% of cases performed under unilateral antegrade selective cerebral perfusion (median time of 40 minutes). Implantation was completed in 96% cases, and the AMDS stent was fully expanded in 97% of implanted patients; the stent did not fully expand in three patients. The likely causes of failed deployment were accidental suture severing during deployment due to mishandling, narrowing due to overly tortuous arch anatomy. Thirty-day follow-up data included 18% mortality, and operation-related new postoperative neurological deficit in 8% of patients. AMDS was able to induce complete or partial thrombosis of the false lumen in the descending aorta in 76% of subjects with adequate imaging, with resolution of pre-operative malperfusion in 80% of the 46 patients. Surgical and/or endovascular reintervention in 13 patients was attributed to persisting malperfusion; in most of these cases a non-covered extension of the AMDS or targeted stenting of aortic branches was performed.

14. ADVERSE EVENT REPORTING

Any adverse event that occurs during the AMDS procedure or after the AMDS implantation should be reported to Artivion Field Assurance at 1-800-438-8285 or by email to fieldassurance@artivion.com, and to the national regulatory authority as applicable.

15. DISCLAIMER OF WARRANTIES; LIMITS OF LIABILITY

ARTIVION DISCLAIMS ALL EXPRESS AND IMPLIED WARRANTIES WITH RESPECT TO THIS DEVICE, INCLUDING BUT NOT LIMITED TO THE EXPRESS AND IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. IN NO EVENT SHALL ARTIVION BE LIABLE FOR INCIDENTAL OR CONSEQUENTIAL DAMAGES. In the event that such disclaimer is found invalid or unenforceable for any reason: (I) any action for breach of warranty must be commenced within one year after any such claim or cause of action accrued and (ii) the remedy for any such breach is limited to the replacement of the product.

16. SYMBOLS USED ON LABELING

	Manufacturer		Use By Date		Keep Dry		Patient Name
	Date of Manufacture		Consult Instruction for Use		Temperature Limit		Date of implantation
	Catalog Number		Sterilized Using Ethylene Oxide		MR Conditional		Name and Address of the implanting healthcare institution/provider
	Batch Code		Do not reuse		Information website for patients		
	Medical Device		Do Not Use If Package Is Damaged		UDI as AIDC format		Do not re-sterilize
	Caution: Federal (USA) Law restricts this device to sale by or on the order of a physician		Sterile barrier system/sterile packaging		Single sterile barrier system with protective packaging outside		Country of Manufacture
	European Authorized Representative		Swiss Authorized Representative		UK Authorized Representative		Importer

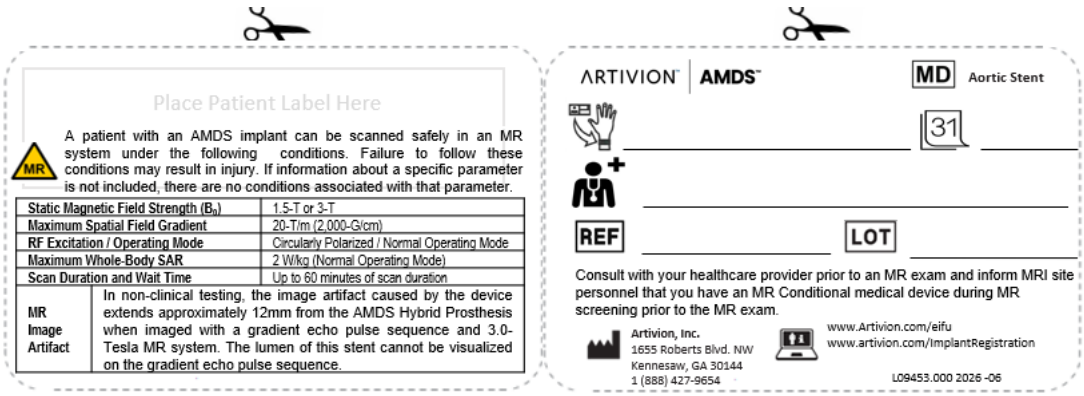
17. PATIENT IMPLANT CARD

Instructions for completion of Patient Implant Card (to be completed by the healthcare institution/provider):

1. Patient name (first, middle, last) or patient ID
2. Date of implantation (YYYY-MM-DD)
3. Name and address of the implanting healthcare institution/provider (two lines)
   Physician's name (last line)
4. Attach one of the device courtesy labels to the implant card

The AMDS Hybrid Prosthesis is packaged with an implant card, all patients should be instructed to keep this card in their possession at all times.

[5] Montagner M, Kofler M, Seeber F, Pitts L, Starck C, Sündermann SH, Kurz S, Grubitzsch H, Falk V, Kempfert J. The arch remodelling stent for DeBakey I acute aortic dissection: experience with 100 implantations. Eur J Cardiothorac Surg. 2022 Jul 11;62(2).



Place Patient Label Here

A patient with an AMDS implant can be scanned safely in an MR system under the following conditions. Failure to follow these conditions may result in injury. If information about a specific parameter is not included, there are no conditions associated with that parameter.

Static Magnetic Field Strength (B_0)	1.5-T or 3-T
Maximum Spatial Field Gradient	20-T/m (2,000-G/cm)
RF Excitation / Operating Mode	Circularly Polarized / Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg (Normal Operating Mode)
Scan Duration and Wait Time	Up to 60 minutes of scan duration
MR Image Artifact	In non-clinical testing, the image artifact caused by the device extends approximately 12mm from the AMDS Hybrid Prosthesis when imaged with a gradient echo pulse sequence and 3.0-Tesla MR system. The lumen of this stent cannot be visualized on the gradient echo pulse sequence.

ARTIVION | AMDS™ MD Aortic Stent

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REF LOT

Consult with your healthcare provider prior to an MR exam and inform MRI site personnel that you have an MR Conditional medical device during MR screening prior to the MR exam.

Artivion, Inc.
1655 Roberts Blvd. NW
Kennesaw, GA 30144
1 (888) 427-9654

www.Artivion.com/eifu
www.artivion.com/ImplantRegistration

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18. IMPLANT REGISTRATION

Regulatory agencies require the tracking of the AMDS™ Hybrid Prosthesis (AMDS). Artivion requests that patient implant registration is completed. The instructions and form for completing the patient implant registration is provided on the Artivion website at: www.artivion.com/ImplantRegistration. All patient information remains strictly confidential, and the release of patient-identifying information can be refused by law.