SUMMARY OF SAFETY AND PROBABLE BENEFIT (SSPB)

I. GENERAL INFORMATION

Device Generic Name: Vascular stent for open surgical placement, thoracic aortic dissection treatment

Device Trade Name: AMDS™ Hybrid Prosthesis

Device Procode: QSK

Applicant's Name and Address: Artivion, Inc.
1655 Roberts Blvd. NW
Kennesaw, GA 30144

Date(s) of Panel Recommendation: None

Humanitarian Device Exemption (HDE) Number: H230007

Humanitarian Use Device (HUD) Designation Number: HUD # DEV-2017-394

Date of HUD Designation: December 11, 2017

Date of Notice of Approval to Applicant: December 4, 2024

II. 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.

III. 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

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AMDS™ Hybrid Prosthesis labeling.

V. DEVICE DESCRIPTION

The AMDS™ Hybrid Prosthesis (AMDS) is an implantable, uncovered stent constructed from braided Nitinol wire, attached proximally to a polytetrafluoroethylene (PTFE) felt cuff with polyester (PET) sutures (***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 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.

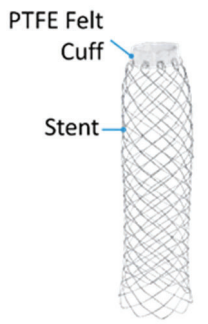

Figure 1. The AMDS Implant

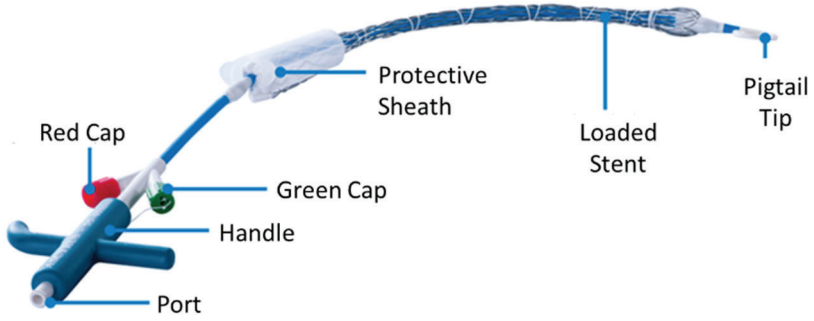

Figure 2. The AMDS Delivery System

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 cuff is used to strengthen the distal aortic anastomosis created between a conventional polyester graft and the transected aorta. The main function of the 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 is offered in eight configurations based on the stent sizing to fit a range of aortic diameters and lengths (see **Table 1**). The 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 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)**			
AMDS 40	Straight	20-35	25-35	153	207	24	527	135
AMDS 40c						28		
AMDS 4030	Tapered		20-24	159	203	24		
AMDS 4030c						28		
AMDS 55	Straight	36-45	36-45	187	215	32	565	150
AMDS 55c						28		
AMDS 5540	Tapered		27-35	185	211	32	546	145
AMDS 5540c						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

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for treatment including medical management or conventional open surgical including ascending/hemiarch repair or more extensive total arch repair, with or without a frozen elephant trunk (FET). Each alternative has its own advantages and disadvantages. A patient should fully discuss the advantages and disadvantages of each option with their physician to select the treatment method that will be best suited for their particular condition and lifestyle, considering the benefits and risks of treatment.

VII. MARKETING HISTORY

The AMDS is commercially available in the countries listed in ***Table 2***. The AMDS has not been withdrawn from marketing for any reason relating to the safety and probable benefit of the device**.**

Table 2. AMDS Marketing History

Europe, Middle East, and Africa				
Austria	Estonia	Italy	Kuwait	Slovakia
Belgium	Finland	Latvia	Malta	Spain
Bulgarian	France	Germany	Netherlands	Sweden
Croatia	Hungary	Greece	Norway	Switzerland
Cyprus	Iceland	Liechtenstein	Poland	Turkey
Czech Republic	Ireland	Lithuania	Romania	United Kingdom
Denmark	Israel	Luxembourg	Serbia	---
North and South America				
Canada		Chile	Dominican Republic	Columbia	Mexico
Costa Rica		Panama	Peru	Venezuela	---
Asia Pacific				
Australia		Hong Kong		Malaysia
New Zealand		Singapore		Thailand

VIII. PROBABLE ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects (i.e., complications) associated with the hemiarch repair procedure with use of the AMDS include, but are not limited to:

Table 3. Potential Adverse Events

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

IX. SUMMARY OF NON-CLINICAL STUDIES

Non-clinical studies were completed to evaluate the AMDS, including non-clinical bench testing, biocompatibility, sterilization, packaging, and shelf-life.

A. LABORATORY STUDIES

The AMDS underwent testing for design verification and validation as shown in ***Tables 4-8***. Testing was performed in accordance with ISO 25539-1:2017 *Cardiovascular implants -- Endovascular devices --Part 1: Endovascular prostheses*. Test samples were selected either as a worst-case sample due to device attributes (e.g., for dimensional attributes such as largest/longest stent or delivery system), or as representative (e.g., for design or performance attributes which remain the same among models).

Table 4. Non-Clinical Testing (Stent and Delivery System)

Test Name	Test Purpose	Acceptance Criteria	Results
Simulated Use Testing[+]*	To evaluate the preparation, insertion, delivery, deployment, and withdrawal of the AMDS in an anatomical model under simulated use conditions.	Delivery system must be able to be flushed, pass a 0.035" guidewire, track through the anatomical model, deploy the stent in the intended location, and were withdrawn without difficulty, with a maximum deployment force ≤ 25 N. The stent must conform to the vessel wall and tack the simulated dissection flap for closure of the false lumen.	Pass
Corrosion and Nickel Ion Release Testing[+]	To evaluate the corrosion resistance properties of the stent.	The device must not corrode under anticipated in-vivo conditions, and/or the nickel release profile must demonstrate the device has a stable surface oxide under real-time immersion conditions.	Pass
Implant Foreshortening[+]	To evaluate the change in length of the stent from its crimped state to its expanded state.	The minimum stent length should be ≥ 12 cm (120mm) upon deployment in a curved vessel model.	Pass

[+] Testing conducted with samples at t=0,
*Testing conducted using aged samples.

Table 5. Non-Clinical Testing (AMDS Implant)

Test	Test Purpose	Acceptance Criteria	Results
Dimensional Verification[+]*	To evaluate the stent for conformance to visual and dimensional specifications (conducted only within the 3-year shelf life study).	Implant Evaluation There should be no visual defects (e.g., broken strut, crack, scrape/loss of strut thickness >10%, deformation of stent). The stent free surface area (SFSA) must be ≥ 95.0% for all AMDS models. The stent nominal outer diameter (OD) and felt cuff must be within the tolerance for each size and cuff type:	Pass

Stent OD (mm)	Min	Max
30	25	37
40	35	47
55	47	65

Table 5. Non-Clinical Testing (AMDS Implant)

Test	Test Purpose	Acceptance Criteria	Results
		<table><tr><th colspan="2">Cuff OD (mm)</th></tr><tr><td>AMDS40c / AMDS4030c AMDS55c / AMDS5540c</td><td>28 ± 2</td></tr><tr><td>AMDS40 / AMDS4030</td><td>24 ± 2</td></tr><tr><td>AMDS55 / AMDS5540</td><td>32 ± 2</td></tr></table> Stent length varies based on the nominal stent diameter and was measured for characterization only.	
Cuff Attachment Strength+*	To verify the felt cuff is securely attached to the stent.	The felt to stent attachment strength should be ≥ 40N.	Pass
Crush Resistance+*	To evaluate the stent diameter recovery after compression.	Stent must have <10% change in recovered free-state diameter after compression to 50% of its original free state diameter.	Pass
Stent Kink Resistance+	To evaluate the stent for kinking.	Stent must not kink or have a diameter reduction greater than 50% compared to free state when deployed in a 1" radius.	Pass
Chronic Outward and Radial Resistive Forces+*	To characterize the radial outward and resistive forces of the AMDS stent.	Radial resistive force at smallest treatment diameter is greater than 2.017 N/cm. Chronic outward force at smallest treatment diameter is less than 5 N/cm (linear) to avoid damage to the aortic wall.	Pass
MRI Testing+	To evaluate the MRI scanning conditions for the AMDS stent.	A patient with an AMDS stent can be scanned safely in an MR system under the following conditions: • For characterization of MR Safety only. *Static magnetic field of 1.5-Tesla and 3-Tesla, only* • *Maximum spatial gradient magnetic field of 2,000-gauss/cm (20-T/m)* *Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2-W/kg for 60 minutes of scanning (i.e., per pulse sequence) in the Normal Operating Mode*	MR Conditional
Fatigue and Durability – Computational Analysisϒ	FEA was used to analyze the material strains within the stent.	FEA simulations demonstrated a fatigue safety factor > 1 when compared to the fatigue safety limit and identified the worst-case AMDS stent for in vitro fatigue testing.	Pass
Pulsatile Fatigue Testing – In vitro testing+	To evaluate fatigue life of the stent under pulsatile loading for 400 million cycles.	No fractures which cause a section of the stent to detach (e.g., a clinically meaningful fracture of the continuous braided stent wire which would compromise stent radial force) shall occur after 400 million cycles in both straight and bent configurations. No fractures which cause a section of the stent to detach shall occur after 400 million cycles.	Pass

+ Testing conducted with samples at t=0,
***Testing conducted using aged samples,**
ϒ No physical samples, computational only.

Table 6. Non-Clinical Testing (AMDS Delivery System)

<table>
<tr><th>Test Name</th><th>Test Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td>Dimensional Verification+*</td><td>To evaluate the delivery system for conformance to visual and dimensional specifications (conducted only on samples in a 3-year shelf life study).</td><td><u>Delivery System Evaluation</u>
The Delivery System must be free of significant kink, cuts, cracks, or deformed bumps. The delivery system dimensions should be within the following specifications:
- Catheter shaft outer diameter (OD) ≤ 0.394 inches
- Guidewire Lumen inner diameter (ID) ≥ 0.040 inches
- Stent Loading Length:
<table><tr><th>Stent Loading Length (mm)</th><th>Min</th><th>Max</th></tr><tr><td>AMDS40 and AMDS40-30</td><td>235</td><td>245</td></tr><tr><td>AMDS55</td><td>280</td><td>290</td></tr><tr><td>AMDS55-40</td><td>260</td><td>270</td></tr></table>- Working length
<table><tr><th>Working Length (mm)</th><th>Min</th><th>Max</th></tr><tr><td>AMDS40 and AMDS40-30</td><td>425</td><td>445</td></tr><tr><td>AMDS55</td><td>463</td><td>483</td></tr><tr><td>AMDS55-40</td><td>444</td><td>464</td></tr></table></td><td>Pass</td></tr>
<tr><td>Tensile and Torsional Bond Strength+*</td><td>To evaluate tensile and torsional bond integrity of the delivery catheter after simulated use.</td><td>Each bond joint of the catheter must have a tensile strength ≥ 15N and must not fail when rotated 180° in any direction.</td><td>Pass</td></tr>
</table>

+ Testing conducted with samples at t=0.
*Testing conducted using aged samples.

B. BIOCOMPATIBILITY STUDIES

The biological evaluation of the AMDS was conducted in accordance with *ISO 10993-1:2018 Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process* and *FDA Guidance, Use of International Standard ISO 10993-1.*

Per ISO 10993-1:2018 guidelines, the AMDS Implant is considered a permanent implant device (contact duration >30 days) in contact with circulating blood. The results of the biocompatibility testing performed for the AMDS Implant are summarized in ***Table 7.*** All biocompatibility testing was conducted with unaged (t=0) test samples.

Table 7. Biocompatibility Evaluation - AMDS Implant

Test	Purpose	Results
ISO MEM Elution Method Cytotoxicity	To determine potential cytotoxicity when L-929 mouse fibroblast cells are exposed to implant extracts.	**Pass** Non-cytotoxic
ISO Guinea Pig Maximization Sensitization	To evaluate the potential allergenic/ sensitization potential of implant extracts in guinea pigs.	**Pass** Non-sensitizing
ISO Intracutaneous Reactivity	To evaluate the potential irritation effects after intracutaneous injection of implant extracts in rabbits.	**Pass** Non-irritating.
ISO Material Mediated Pyrogenicity	To evaluate implant extracts for the potential of inducing a pyrogenic response in rabbits.	**Pass** Non-pyrogenic

Table 7. Biocompatibility Evaluation - AMDS Implant

Test	Purpose	Results
ASTM Hemolysis Assay (Direct)	To evaluate the potential of the implant to cause hemolysis in direct contact or by extraction.	**Pass** Non-hemolytic
Sc5b-9 Complement Activation Assay	To determine the potential of the implant to activate complement.	**Pass** The test article was not considered to be a potential activator.
Implantation Intramuscular (4 Weeks)	To evaluate the local tissue response after the test implant is implanted in muscle tissue in rabbits.	**Pass** The macroscopic reaction was not significant. The test article caused minimal/no reaction compared to the negative control article.
ISO Muscle Implantation with Histopathology- 13 Weeks	To evaluate the local tissue response after the test implant is implanted in muscle tissue in rabbits.	**Pass** The macroscopic reaction was not significant as compared to the negative control article. Microscopically, the test article caused a minimal or no reaction as compared to the negative control article.

In Vivo Thrombogenicity was not tested based on the use of known materials and results of the DARTS Clinical Study.

The AMDS Delivery System is not placed directly in circulating blood (as blood flow is stopped during transection of the aorta while undergoing hemiarch repair) but is considered an externally communicating device which comes in contact with residual blood in the aorta for a limited contact duration (< 24 hours). The results of the biocompatibility testing performed for the AMDS Delivery System is summarized in ***Table 8***. All biocompatibility testing was conducted with unaged (t=0) test samples.

Table 8. Biocompatibility Evaluation for the AMDS Delivery System

Test	Purpose	Results
ISO Mem Elution Method Cytotoxicity	To determine if cytotoxicity is caused when L-929 mouse fibroblast cells are exposed to implant extracts.	**Pass** Non-cytotoxic
ISO Guinea Pig Maximization Sensitization Test	To evaluate the allergenic/sensitization potential of implant extracts in guinea pigs.	**Pass** Non-sensitizing
ATSM Hemolysis Assay (Direct)	To evaluate the potential of the implant to cause hemolysis in direct contact or by extraction.	**Pass** Non-hemolytic
USP Material Mediated Pyrogenicity	To evaluate implant extracts for the potential of inducing a pyrogenic response in rabbits.	**Pass** Non-pyrogenic
ISO Acute Systemic Injection Test	To evaluate the potential toxic effects after single-dose systemic injections of implant extracts in mice.	**Pass** None of the test article treated animals were observed with clinical signs consistent with toxicity at any of the observation periods.
ISO Intracutaneous Reactivity	To evaluate the potential irritation effects after intracutaneous injection of implant extracts in rabbits.	**Pass** Non-irritating
ISO SC5b9 Complement Activation Test	To determine the potential of the implant to activate complement.	**Pass** The test article was not considered to be a potential activator of the complement system.

The AMDS has not been tested to establish potential of systemic toxicity, genetic toxicity, and carcinogenicity. Prolonged exposure to systemic, genetic, or carcinogenic toxicants may lead to long term tissue harm and long term mutagenic and carcinogenic affects. The risks of these potential harms from the product have not been established clinically.

C. Sterilization, Packaging and Shelf Life

The AMDS is a single-use device that is provided sterile to the end user. It is sterilized using Ethylene Oxide (EO) gas in accordance with ISO 11135 *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*. The sterilization study confirms that the sterilization Assurance Level (SAL) of 10^{-6} is assured per sterilization plan. The ethylene oxide sterilization residuals were validated and analyzed according to ISO 10993-7. A validated aeration cycle ensures EO, ethylene cholorohydrin (ECH) and ethylene glycol (EG) residues on the sterilized products are below the limits in accordance with ISO 10993-7 *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*.

The packaging validation study was conducted to demonstrate AMDS packaging integrity in conformance with ISO 11607-1:2019 to support the claimed shelf life of 3 years. A total of 59 test articles were subjected to at least one ethylene oxide (EO) sterilization cycles and to environmental conditioning per ASTM D4332 *Standard Practice for Conditioning Containers, Packages, or Packaging Components for Testing*, and ASTM D4169 (DC13) *Standard Practice for Performance Testing of Shipping Containers and System*. The following package integrity testing was conducted to demonstrate sterile barrier integrity with 95% confidence and 95% reliability:

- Visual Inspection in accordance with ASTM F1886/F1886M was performed for all 59 samples and found no observable damage to the sterile barrier, the tray-lid seal was uniform, and the product was secured as intended in the tray.
- Bubble Leak Testing in accordance with ASTM F2096 Annex B was performed for all 59 samples; no unit exhibited gross bubble leaks (e.g., seal channels, pinholes, cracks or tears).
- Seal Peel Testing in accordance with ASTM F88/F88M was performed using 30 samples to demonstrate a minimum tray-lid seal peel force ≥ 1bf on using samples taken from all four sides of the tray. All samples met the minimum seal strength.

The AMDS packaging configuration used in these studies reflects the final package configuration.

D. Animal Study

A non-GLP porcine study of the AMDS™ Hybrid Prosthesis was conducted. The endpoints of this feasibility study were to objectively evaluate the proposed surgical approach for AMDS stent implantation in an animal model, and to identify any immediate and short-term safety concerns. A shorter version of the AMDS stent (40mm diameter x 50mm length) was created with the intention of staying true to the AMDS design intended for human implants, acknowledging that the AMDS™ Hybrid Prosthesis intended for human use is excessively

oversized to the porcine aorta. In the 2 study animals, a mismatch of the device-to-aorta size was observed, as a minimum 20-25mm vessel diameter required for AMDS implantation exceeds that of the typical vessel diameters (16-9mm) in animal models. It was concluded that the animal ascending aorta and aortic arch anatomy is inappropriate for the intended open implantation of the AMDS, as the short ascending segment of the aorta makes the delivery of the AMDS as intended for human use very difficult and unsuccessful. The open surgical technique to place the AMDS in these animals would not allow for the implantation of the device without performing a total arch replacement, which is technically difficult, not clinically relevant and may result in excessive animal morbidity. Therefore, due to the stated animal model limitations, rather than performing a GLP large animal study, existing clinical data was leveraged to address relevant in vivo safety endpoints, along with other available data (bench and biocompatibility data) to address relevant in vivo safety endpoints.

X. SUMMARY OF CLINICAL INFORMATION

The applicant performed clinical studies in the United States (PERSEVERE, NCT # NCT05174767) and in Canada and Europe (DARTS I Study, NCT # NCT03397251, NCT03035643) to establish a reasonable assurance of safety and probably benefit for treatment of patients with Acute DeBakey I dissections with the AMDS as an adjunct to conventional surgery (e.g., ascending/hemiarch repair). The 30-day data from the PERSEVERE IDE study and the 3-year data from the DARTS investigational clinical study were the basis for HDE approval decision. A summary of the PERSEVERE Pivotal IDE and DARTS I investigational clinical study is presented below, along with additional supplemental clinical data supporting the safety of the AMDS in real-world use. In this HDE, clinical data was not leveraged to support approval of a pediatric patient population.

A. SUMMARY OF CLINICAL STUDY (PERSEVERE)

1.1.1. 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. A total of 93 patients were included in the study; the first patient was enrolled in July 2022 and the last patient was enrolled in November 2023 and 26 sites participated within the United States. 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. Data used in this analysis was exported on 22-Dec-2023. This includes complete, 30-day adjudicated follow-up data of 78 subjects for the primary endpoint analysis; secondary endpoint data and longer term data is not yet completely adjudicated. No analyses were performed for [sex-, gender-, age-, race-, ethnicity-, or any other relevant characteristic- specific] subgroups.

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% derived from published clinical outcomes after the standard of care (hemiarch procedure), calculated as the average of the 5 estimations for the total number of patients with at least one in-hospital MAE in the malperfusion reference cohort[1]. Sample size was calculated assuming enrollment of 93 patients with an expected drop-out rate of 10% at 30-days, which would leave 84 patients required 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 ≤ 30days post-procedure. The results will be tested against a performance goal of 45% derived from the weighted average of published DANE rates after the standard of care (hemiarch procedure) as reported in the DANE reference cohort[2]. Sample size was calculated assuming a minimum of 21 patients required to achieve the statistical assumptions under an assumed true AMDS 30-day rate of 10%.

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

To support the HDE approval, a preliminary analysis was conducted to establish an assurance of safety and probable benefit based upon the co-primary endpoints stated above using 30-day follow-up data in all 93 patients enrolled in the PERSEVERE study. External evaluation groups used during the PERSEVERE study included:

- A 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 in the 30-day analysis.
- An external Clinical Events Committee (CEC) adjudicated co-primary endpoint events and select adverse events.

1. Inclusion and Exclusion Criteria

The patient population included patients who were ≥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 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

[1] Bossone et al., Geirsson et al., Girdauskas et al., Pacini et al, Zindovic et al.
[2] Bing et al., Ergin et al., Rylski et al., Tamura et al.

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
- 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)

2. Schedule of Assessments

Patients were evaluated at baseline for study eligibility, monitored from the start of the procedure through discharge, and followed per the study protocol as shown in ***Table 9*** .

Table 9. 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	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]

*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; * indicates per site based on standard of care*

3. Clinical Endpoints

The co-primary endpoints which demonstrate a reasonable assurance of safety and probable benefit to support HDE approval include the following:

- Patients experiencing at least one of the following major adverse events (MAEs): all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, myocardial infarction ≤ 30-days post-procedure. 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 PERSEVERE pivotal study preliminary main analysis supporting an HDE approval decision was considered successful if the lower limit of the 95% confidence interval, associated with the proportion of patients who experience at least one MAE (all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, or myocardial infarction) at 30-days post procedure is less than 58%, and the lower limit of the of the 95% confidence interval associated with the proportion of patients who experience a DANE tear at 30-days post procedure is less than 45%.

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 branch vessel patency and their corresponding 95% exact (Clopper-Pearson) confidence intervals will be reported. 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
    - 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

The secondary 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 visit.

- Analysis of Secondary Composite Endpoints of technical and procedural success rates and their corresponding 95% exact (Clopper-Pearson) confidence intervals were reported, as defined below:
    - *Technical Success at conclusion of the index procedure*: 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*: 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, and distal procedure-related thromboembolic events, and any additional unplanned surgical or interventional procedures related to the device since completion of the original procedure.

4. Patient Accountability and Compliance to Follow-Up

At the time of analysis, pre-procedure and procedure data was available for all 93 enrolled patients, with 30-day post-operative data available for 78 patients. Currently, 15 patients have died, and one patient withdrew from the study. Subject status and data availability is shown in ***Table 10***.

Table 10. PERSEVERE Subject Status, Follow-Up Compliance and Imaging Quality Summary

Visit Details		Subjects with Data for Visit and Subject Status						Imaging Compliance and Quality to Assess Parameters of Interest[5]		
Visit #	Visit Description	Eligible for follow-up[1]	Subjects with Data for Visit	Subjects with Visit Missed or Pending	Death Prior to Indicated Visit	LTF/ Withdrawn Prior to Indicated Visit	Not due for next visit[4]	CT/CTA read by Core Lab	TL Diameter at Zone 3	DANE
		#	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)
1	Pre-Op	93	93/93 (100%)	0/93 (0%)	NA	NA	NA	91/93 (97.8%)	89/93 (95.7%)	NA
2	Procedure	93	93/93 (100%)	0/93 (0%)	0/93 (0%)	0/93 (0%)	0 (0%)	NA	NA	NA
3	30-days[2]	93	78/93 (83.9%)	6/93 (6.5%)	9/93 (9.7%)	0/93 (0%)	9/93 (9.7%)	68/93 (73.1%)	63/93 (67.7%)	61/93 (65.6%)
4	31-180 days[3]	75	54/75 (72.0%)	18/75 (24.0%)	3/75 (4.0%)	0/75 (0%)	54/75 (72.0%)	43/75 (57.3%)	41/75 (54.7%)	41/75 (54.7%)
5	181-365 days	18	9/18 (50%)	5/18 (27.8%)	3/18 (16.7%)	1/18 (5.6%)	9/18 (50.0%)	6/18 (33.3%)	6/18 (33.3%)	5/18 (27.8%)

[1] Eligible for follow-up = eligible for follow-up from the previous interval – [death+LTF+not due for next visit]

[2] This time period includes >24 hours post-procedure through 30-days; the CTA data indicates data available within the 30-day visit window.

[3] Subjects pending includes those within the window who did not have data entry at time of data export.

[4] Those subjects that are "Not due for next visit" are those subjects that are not within the follow-up window for the next interval.

[5] The data represents the existence of available data; these numbers do not reflect incidence of reported events.
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

5. Study Population Baseline Characteristics

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 58.6 ± 9.45 years and average body mass index (BMI) of 29.69 ± 7.18 kg/m^2). All patients presented with preoperative clinical (80%) or radiographic (20%) malperfusion syndrome in at least one organ system. Comorbidities most commonly included history of coronary artery disease (CAD) (11.8%), cardiac arrhythmia (20.4%) and prior myocardial infarction (3.2%), diabetes (15.1%), and chronic obstructive pulmonary disease (COPD) (10.8%) (see ***Table 11***).

Table 11. Patient Baseline Characteristics (PERSEVERE)

Characteristics	**Total Patients (n=93)**
Demographics and Baseline Characteristics	
Age	58.6 ± 9.45
% Male	78.5%
Preoperative Clinical / Radiographic Malperfusion	80% clinical / 20% radiographic
Race	
Asian	1 (1.1%)
Black or African American	21 (22.6%)
White	56 (60.2%)
Unknown or missing	14 (15.1%)
Ethnicity	
Non-Hispanic	73 (78.5%)
Hispanic or Latino	10 (10.8%)
Unknown or missing	10 (10.8%)
Aortic Arch Anatomy	
Normal (3 great vessels)	66 (71.0%)
Bovine Arch	21 (22.6%)
Isolated Vertebral	5 (5.4%)
Not documented/assessed	2 (2.2%)
Primary entry tear in Zone 0 documented by Core Lab	92.5% (86)
Primary entry tear in Zones 1-3 documented by Core Lab	4.3% (4)
Primary entry tear data missing	3.2% (3)
Risk Factors – No of Patients (%)	
Cardiac Arrhythmia	20.4% (19)
Congestive Heart Failure (CHF)	4.3% (4)
Coronary Artery Disease (CAD)	11.8% (11)
Chronic Pulmonary Obstructive Disease (COPD)	10.8% (10)
Peripheral Arterial Disease	0% (0)
Hypertension	45 (48.4%)
Liver Disease	5 (5.4%)
Cancer	11 (11.8%)
Chronic Renal Insufficiency requiring dialysis	1 (1.1%)
Diabetes	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	0% (0)
Prior PCI	5 (5.4%)
Previous Cardiac Intervention – Other	4 (4.3%)

5. *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 12***.

Table 12. Procedural Characteristics (PERSEVERE)

Procedural Characteristics		**N (% Patients)**
Concomitant Procedures	None (Hemiarch + AMDS only)	13 (14.0%)
	Aortic Root Repair or Replacement	35 (37.6%)
	Aortic Valve Repair or Replacement	21 (22.6%)
	Coronary Artery Bypass Surgery (CABG)	5 (5.4%)
	Other	24 (25.8%)
		Median (Range)
Procedure Times (minutes)	AMDS Deployment Time (min)	4 (0-11)
	Cardiopulmonary Bypass (CPB) Duration Time (min)	175.5 (91-403)
	Hypothermic Circulatory Arrest (min)	28 (0-168)
	Cerebral Perfusion Time (min)	28 (10-230)
	Total AMDS Implantation Time (min)	15 (5-277)

- *Co-Primary Endpoints*

Complete, adjudicated data included in the co-primary endpoint for major adverse events (MAE) occurring within 30 days post-procedure are shown in ***Table 13***. The imaging Core Lab found 0 DANE tears (95% CI: 0%, 3.9%) in any of the 61 CTAs which were evaluated at Visit 3 (30-days) and had sufficient quality to analyze the image and which met the minimum sample size (21 patients) required to meet the statistical assumptions (compared to a performance goal of 45%). The co-primary endpoints were met based upon the 30-day data. Patients experiencing at least one of the following MAEs was 28.0% (95% CI: 18.7%, 37.2%) compared to the performance goal of 58%.***Table 13. Major Adverse Events – Adjudicated (PERSEVERE)***

Major Adverse Events	**Total Number of Events Adjudicated (% Patients)**
All-cause Mortality	9 (9.7%)
New Disabling Stroke*	11 (11.8%)
New Onset Renal Failure Requiring Dialysis	18 (19.4%)
Myocardial Infarction	0 (0%)
Total # of Patients with ≥ 1 MAE	**26 (28.0%)**
# of Patients with Distal Anastomotic New Entry (DANE) Tear	0 (0%)

*New disabling stroke (defined as a change in the modified Rankin Score (mRS) > 2, with a change from baseline > 1).

6. *Secondary Endpoints*

The following MAEs were observed at any point in follow-up (listed from most to least observed, with adjudicated rates for events requiring adjudication): new onset of renal failure requiring dialysis (18.3%), respiratory failure (18.3%), new post-operative organ malperfusion (14%), new disabling stroke (8.6%), new non-disabling stroke (2.3%), thromboembolic events (8.6%), bowel ischemia (2.2%), and myocardial infarction (2.2%). Aortic rupture, pseudoaneurysm, hypersensitivity, new post-operative paraplegia or paraparesis, recurrent laryngeal or phrenic nerve injury, and severe heart failure requiring mechanical circulatory

support were not observed. There were no unanticipated device-related reoperations and no explants. Considering all CTAs evaluated by the imaging Core Lab, there was no radiographic evidence of DANE, distal stent induced new entry (d-SINE) tear, device migration, stent fracture, kink, or twist.

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; 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 80.9% (n = 72 of 89 patients) of patients who had a 30-day visit completed and/or patients who had an MAE ≤ 30 days from the AMDS procedure. Four patients in total were missing data. Seventeen patients did not achieve procedural success for the following reasons: 9 patients died, 7 patients had a 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. or distal procedure-related thromboembolic event. There were also no additional unplanned procedures related to the device within 30-days. Procedural success information was not available for 4 patients at the time of data export. There were no subgroup analyses conducted for the PERSEVERE study.

7. *Aortic Remodeling through 30-Day Follow-Up*

The aorta was analyzed at aortic zones 1-3 to evaluate the change in maximal total aortic diameter, true lumen and false lumen diameter (***Table 14***), as well as false lumen status (***Table 15***). Aortic zones were defined by the Society of Thoracic Surgeons (STS) Society of Vascular Surgeons (SVS) Aortic Zone Classification (see ***Figure 3***). The number of scans for each endpoint at each timepoint varied due to CTA quality issues, as well as anatomical and implant variations.

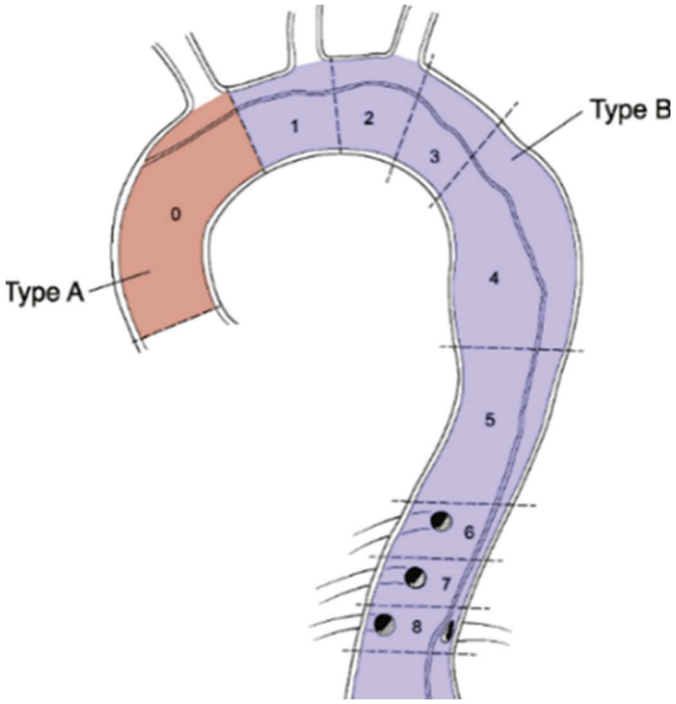

Figure 3. STS/SVS Aortic Zone Classification

Table 14. Aortic Remodeling – Change from Baseline through 30-Day Follow-Up [Mean (SD)]

Aortic Zone	Total Aortic Diameter		True Lumen Diameter		False Lumen Diameter (mm)	
	Discharge (n=48)	30-Days (n=68)	Discharge (n=48)	30-Days (n=68)	Discharge (n=48)	30-Days (n=68)
Zone 1	0.50 (2.923)	0.47 (3.331)	11.22 (4.973)	12.21 (4.931)	10.74 (4.259)	-11.34 (6.207)
Zone 2	0.86 (3.057)	1.34 (3.651)	11.34 (4.361)	12.08 (4.901)	-10.39 (4.790)	-10.69 (5.426)
Zone 3	1.73 (2.290)	3.32 (3.319)	5.92 (4.527)	6.72 (5.376)	-4.27 (4.716)	-3.37 (5.921)

Values for (n) per visit indicate the highest number of patients with data for that visit across all zones, as measurement availability can vary by zone; availability of change data may be less than what is indicated.

Table 15. Aortic Remodeling – Change from Baseline at Discharge and 30-Day Follow-Up [n (%)]

Aortic	Discharge (n=71)				30-Days (n=69)			
FL Status	Completely Thrombosed	Partially Thrombosed	Patent	Not Assessed	Completely Thrombosed	Partially Thrombosed	Patent	Not Assessed
Zone 1	9 (9.7%)	21 (22.6%)	1 (1.1%)	40 (43.0%)	11 (14.1%)	29 (37.2%)	10 (12.8%)	19 (24.4%)
Zone 2	8 (8.6%)	27 (29.0%)	6 (6.5%)	30 (32.3%)	7 (9.0%)	41 (52.6%)	12 (15.4%)	9 (11.5%)
Zone 3	6 (6.5%)	28 (30.1%)	7 (7.5%)	30 (32.3%)	4 (5.1%)	46 (59.0%)	10 (12.8%)	9 (11.5%)
Zone 4	2 (2.2%)	35 (37.6%)	5 (5.4%)	29 (31.2%)	0 (0.0%)	50 (64.1%)	9 (11.5%)	10 (12.8%)
Zone 5	2 (2.2%)	31 (33.3%)	8 (8.6%)	30 (32.3%)	0 (0.0%)	45 (57.7%)	13 (16.7%)	11 (14.1%)

B. SUMMARY OF ADDITIONAL CLINICAL STUDY (DARTS I)

The DARTS I Study is a prospective, single-arm, multi-center study of the AMDS for treatment of patients with Acute DeBakey I dissections. A total of 46 patients met the protocol eligibility criteria and were enrolled at 5 sites in Canada (n=39) and 1 site in Germany (n=7) over a period spanning approximately 2 years (between March 2017 and January 2019). Patients are to be followed for 5 years. The results of the study were compared to literature-based results reported for ascending/ hemiarch repair using descriptive statistics. An independent core laboratory evaluated the imaging obtained during the study, including true lumen and total aortic diameter measurements, false lumen status, and the presence of re-entry tears. The study did not include a Clinical Events Committee nor a Data Safety Monitoring Board. No analyses were performed for [sex-, gender-, age-, race-, ethnicity-, or any other relevant characteristic- specific] subgroups.

1. Inclusion and Exclusion Criteria

The study population included patients with acute DeBakey Type I aortic dissection. Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

- ≤18 years of age or over 80 years of age
- Life expectancy less than 2 years
- Uncontrolled systemic infection
- Patient in extreme hemodynamic compromise requiring cardiopulmonary resuscitation (CPR)
- Inability to obtain CT angiograms for follow-up
- Patients previously diagnosed with Marfan syndrome, Ehlers- Danlos syndrome or Loeys- Dietz syndrome based on laboratory genetic testing on a date prior to the diagnosis of the dissection
- Any pathology of mycotic origin
- Subacute or chronic dissection (>14 days after the index event)
- Aortic fistulous communication with non-vascular structure (e.g., esophagus, bronchial)
- Extensive thrombus or calcifications in the aortic arch
- Excessive tortuosity precluding safe passage of the AMDS
- Descending thoracic aneurysm involving the proximal third (1/3) of the descending aorta and measuring > 45 mm in diameter.
- Aortic arch aneurysm > 45 mm in diameter (Germany only)

2. Schedule of Assessments

Patients were evaluated at baseline for study eligibility, monitored from the start of the procedure through discharge, and followed per the study protocol as shown in ***Table 16***. Imaging included CT/CTA scans.

Table 16. DARTS I Study Visit Schedule of Assessments

PROTOCOL ACTIVITIES	Pre-Op[1]	Procedure	Post-Procedure (Discharge)	4-6 Weeks Post-Op[2] (+/- 2 weeks)	12 Weeks Post-Op (+/-2 weeks)	24 Weeks Post-Op (+/- 4 weeks)	1-5 Years (+/- 8 weeks)
Informed Consent	X						
Inclusion/Exclusion	X						
Demographics	X						

Table 16. DARTS I Study Visit Schedule of Assessments

PROTOCOL ACTIVITIES	Pre-Op[1]	Procedure	Post-Procedure (Discharge)	4-6 Weeks Post-Op[2] (+/- 2 weeks)	12 Weeks Post-Op (+/-2 weeks)	24 Weeks Post-Op (+/- 4 weeks)	1-5 Years (+/- 8 weeks)
Medical History	X						
Risk Assessment	X						
Device Sizing	X						
Assessment Diagnostic[3]	X		X	X	X	X	X
Procedure		X					
Length of Hospital Stay			X				
Neurological Assessment			X	X	X	X	X
Imaging Evaluation	X		X	X	X	X	X
Adverse Events			X[4]				
Device Removal			X[4]				
Study Exit			X[5]				

[1]The pre-op information is collected within 14 days of the procedure
[2]The 4-6 weeks visit was only applicable to sites in Canada
[3]The Assessment Diagnostic form includes the following information: Medications, Blood Pressure, and Blood Work
[4]An adverse event or device removal (i.e., an explant) could happen at any point after the AMDS procedure
[5]Study exit is anticipated to occur at 5-years, post-procedure, but can happen at any point if the patient withdraws, is lost-to-follow, or dies

3. Clinical Endpoints

The primary safety endpoints included device- and procedure-related mortality, neurological complications (stroke, transient ischemic attack, paraparesis, paraplegia), aortic injury associated with AMDS implantation, and aortic arch vessel patency at 30-day and 3-month follow-up.

The primary effectiveness endpoints included successful reattachment of the intimal flap (absence of DANE), thrombosis (partial or complete) of the false lumen, radiographic evidence of false lumen exclusion at all post-operative visits. Successful device deployment was documented at the conclusion of the procedure.

Secondary endpoints included explant rate, device-related reintervention rate, and long-term follow-up of the primary safety endpoints, and device performance assessment evaluated by an imaging Core Lab (e.g., fracture, compression, kink, twist, DANE tears, and d-SINE tears and were assessed at all follow-up visits.

4. Patient Accountability and Compliance to Follow-Up

Data was available for all 47 enrolled patients for 30-day safety assessment, and 46 in the intent to treat group (e.g., the patients who received the AMDS). Subject status and data availability is shown in ***Table 17***. All evaluable patients have completed three-year follow-up.

Table 17. DARTS I Follow-up and Compliance Table

Visit Details			Subjects with Data for Visit and Subject Status					Imaging Adequate to Assess Parameters of Interest[7]		
Visit #	Visit Description	Eligible for follow-up[1]	Subjects with Data for Visit	Subjects with Follow-up Missed or Pending	Death Prior to Indicated Visit	Lost to Follow-up / Withdrawn Prior to Indicated Visit	Not due for next visit[6]	CT/CTA read by Core Lab	TL Diameter at Zone 3	DANE
		#	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)
1	Pre-Op	47	47/47 (100%)	0/47 (0%)	0/47 (0%)	0/47 (0%)	0/47 (0%)	44/47 (93.6%)	40/47 (85.1%)	NA
2	Procedure[2]	47	47/47 (100%)	0/47 (0%)	0/47 (0%)	0/47 (0%)	0/47 (0%)	NA	NA	NA
	Pre-Discharge	39	38/39 (97.4%)	1/39 (2.6%)	7/39 (17.9%)	1/39 (2.6%)	0/39 (0%)	35/39 (89.7%)	33/39 (84.6%)	30/39 (76.9%)
3	4-6 weeks[3]	39	32/39 (82.1%)	7/39 (17.9%)	0/39 (0%)	0/39 (0%)	0/39 (0%)	27/39 (69.2%)	26/39 (66.7%)	25/39 (64.1%)
4	3-months	38	36/38 (94.7%)	2/38 (5.3%)	1/38 (2.6%)	0/38 (0%)	0/38 (0%)	32/38 (84.2%)	31/38 (81.6%)	28/38 (73.7%)
5	6-months[4]	37	30/37 (81.1%)	7/37 (18.9%)	1/37 (2.7%)	0/37 (0%)	0/37 (0%)	25/37 (67.6%)	25/37 (67.6%)	24/37 (64.9%)
6	1-year[5]	36	35/36 (97.2%)	1/36 (2.8%)	1/36 (2.8%)	0/36 (0%)	0/36 (0%)	34/36 (94.4%)	26/36 (72.2%)	26/36 (72.2%)
7	2-years	35	34/35 (97.1%)	1/35 (2.9%)	1/35 (2.9%)	0/35 (0%)	0/35 (0%)	28/35 (80.0%)	27/35 (77.1%)	25/35 (71.4%)
8	3-years	33	33/33 (100%)	0/33 (0%)	0/33 (0%)	2/33 (6.1%)	0/33 (0%)	30/33 (90.9%)	29/33 (87.9%)	28/33 (84.8%)

[1] Eligible for follow-up = eligible for follow-up from the previous interval - (death + LTF + not due).
[2] Procedure considered as time 24 hours from implant.
[3] The protocol in Germany did not include a 4-6 week visit; 7 patients without data were from the Berlin Site and # with CTA for this visit consider just the patients from Canada
[4] 2 additional patients had an X-ray at 6-months
[5] The death prior to Visit 1 is LON-004, who is not included in the per protocol cohort
[6] The data represents the existence of available data; these numbers do not reflect incidence of reported events. TL diameter measurement at Zone 3 selected due to importance in the PERSEVERE IDE study.
[7] Those subjects that are "Not due for next visit" are those subjects that are not within the follow-up window for the next interval
Abbreviations: NA=Not applicable, CT=computed tomography, CTA=computed tomography angiography, TL=true lumen, LTF=lost-to-follow-up, DANE= distal anastomotic new entry, d-SINE= distal stent induced new entry

5. Study Population Baseline Characteristics

A total of 45 patients (97.8%) were enrolled and treated for acute DeBakey type I dissection; one patient with an intramural hematoma was treated. Patients were mostly male (67.4%) with a mean age of 60 ± 12.4 years and average body mass index (BMI) of 29.1 ± 7.1 kg/m^2). Due to the nature of this disease, comorbidities were anticipated (***Table 18***); patients most commonly presented with hypertension (61%), coronary artery disease (CAD) (15%), cardiac arrhythmia (13%), diabetes (13%), and chronic obstructive pulmonary disease (COPD) (13%), reflecting a sick patient population. A minority of patients had a history of cardiothoracic surgery (2.2%), and 35% self-reported any history of smoking.

Table 18 Patient Baseline Characteristics (DARTS I)

Characteristics	**Total Patients (n=46)**
Demographics and Baseline Characteristics	
Age	60 ± 12.4
% Male	67.4%
Preoperative Clinical / Radiographic Malperfusion	56.5%
Race and Ethnicity	
Asian	1 (2.2%)
Black or African American	1 (2.2%)
White	34 (73.9%)
Not reported (not collected in Germany)	10 (21.7%)
Aortic Arch Anatomy	
Normal (3 great vessels)	71.7%
Bovine Arch	15.2%
Primary entry tear in Zone 0	78.3%*
Presence of secondary entry tears	69.6%
Risk Factors – No of Patients (%)	
Cardiac Arrhythmia	6 (13.0%)
Congestive Heart Failure (CHF)	1 (2.2%)
Coronary Artery Disease (CAD)	7 (15.2%)
Chronic Pulmonary Obstructive Disease (COPD)	6 (13.0%)
Peripheral Vascular Disease	1 (2.2%)
Hypertension	28 (60.9%)
Aneurysm	4 (8.7%)
Liver Disease	1 (2.2%)
Cancer	4 (8.7%)
Chronic Renal Insufficiency requiring dialysis	1 (2.2%)
Diabetes (Insulin Dependent)	1 (2.2%)
Prior Stroke	3 (6.5%)
Prior TIA	1 (2.2%)
Prior Myocardial Infarction	4 (8.7%)
Prior Thromboembolic Event (DVT)	3 (6.5%)
Prior CABG	2 (2.2%)
Prior Percutanous Coronary Intervention (PCI)	2 (2.2%)
Previous Cardiothoracic Surgery	2 (2.2%)

*17% of patients had missing data on the primary entry tear location.

6. Procedural Characteristics

Concomitant procedures (considered anything other than the hemiarch repair and AMDS device implantation procedures) were performed in 57% of cases, most commonly aortic valve repair (30%) or aortic root repair or replacement (20%). AMDS implantation was performed with a mean time of 3 minutes, and the majority of devices were implanted without the need for fluoroscopy (98%) and without intravascular ultrasound to identify the true lumen (96%). Successful device deployment was reported in 100% of patients, with no incidence of aortic injury in any patient. A majority (96%) of AMDS devices were implanted proximal to the innominate artery, with 3 patients (7%) requiring supra-aortic branch vessel bypass. The average Intensive Care Unit (ICU) stay was 10 days; time in the ICU was prolonged for 39% of the cohort. ICU stay was considered prolonged, in the opinion of the investigator. The average hospital stay was 23 days. A summary of procedural outcomes is provided in ***Table 19.***

Table 19. Procedural Characteristics (DARTS I)

Procedural Characteristics		**Patients (%)**
Concomitant Procedures	None (Hemiarch + AMDS only)	20/46 (43.5%)
	Aortic arch replacement	2/46 (4.3%)
	Aortic Root Repair or Replacement	9/46 (19.6%)
	Aortic Valve Repair or Replacement	14/46 (30.4%)
	Coronary Artery Bypass Surgery (CABG)	3/46 (6.5%)
	Other	3/46 (6.5%)
Procedure Times (minutes)	AMDS Deployment Time	3.2 (1 – 15)
	CPB Duration Time	227.7 (8-1035)
	Hypothermic Circulatory Arrest	47.7 (0-322)

7. Results of the Primary Endpoints - Major Adverse Events through 3-Year Follow-Up

There were 6 deaths within 30 days of the procedure; one death was attributed to the procedure and no deaths were considered device related (***Table 20***). All event relationships were determined by the investigators. There were 4 additional deaths beyond thirty days, of which one was considered possibly related to the procedure and none were considered device-related.

Table 20. Major Adverse Events (DARTS I) at 30 Days and 3-Years

Major Adverse Events	**30-Days Total Number of Events (%)**	**3-Years Total Number of Events (%)**
All-cause Mortality	6/46 (13.0%)	10/46 (21.7%)
Procedure-related mortality	1/46 (2.2%)	2/46 (4.3%)
All Neurological Events (Stroke or TIA, paraparesis/paraplegia)	10/46 (21.7%)	11/46 (23.9%)
New Stroke or TIA	6/46 (13.0%)	7/46 (15.2%)

A total of 10 patients (23.9%) experienced neurological complications within the first 30 days, including 6 patients who had new stroke (defined as a new disabling or non-disabling stroke in a patient absent of prior stroke or stroke symptoms pre- or peri-procedure). One additional patient had a new ischemic stroke beyond 30 days. No patients experienced DANE through 3-year follow-up.

8. *Secondary Endpoints*

Late mortality, aortic branch vessel patency, thrombosis of the false lumen, and aortic remodeling (true lumen and false lumen diameter change) were assessed prior to discharge, 3-months, 6-months 1-year and 3-years. The number of subjects with imaging adequate to assess imaging-based endpoints was variable given CTA quality issues and/or patient anatomy (e.g., bovine arch patients did not have data for Zone 1). The change in true lumen and false lumen diameter, and change in false lumen thrombosis, were reported based on the maximum number of measurements available in all zones for all available patients at that visit.

- *Other Major Adverse Events through 3-Year Follow-Up*

The most frequently occurring events (out of 184 adverse events) were atrial fibrillation (6%), pleural effusion (6%), acute kidney injury (5%), and stroke (4%). Treatment was provided for 77% of the observed MAEs, and was predominately non-interventional medical treatment (63%), such as pharmaceuticals; 27 events were resolved with surgery (open or percutaneous) and a subset of events (22%) required hospitalization (new or prolonged). Only a small percentage of events were considered as possibly related to the procedure (10%) or to the AMDS (3%), including posterior reversible encephalopathy syndrome, anemia, hypoxic encephalopathy, cerebellar ischemic injury, and severe upper left arm pain. Late mortality rates at 3-years were 21.7% for all patients (15.3% for malperfusion patients and 28.6% for no malperfusion patients). All events were assessed for relatedness to the device and/or procedure by the site investigators.

- *Arch vessel branch patency:*

Pre-operative orifice stenosis or occlusion was documented in 2 of the 7 patients (38%). A majority of patients (85%) had patent arch vessels at all follow-up visits; seven (7) patients (15%) had evidence of orifice stenosis (>50%) in at least 1 vessel during follow-up potentially caused by chronic conditions leading to calcification build up, coverage by the dissection flap, thrombus related to the dissection, and obstruction by an implanted device. There were no adverse events that were documented in relationship to the observed arch branch vessel orifice stenosis. No arch branch vessels were occluded through 3-year follow-up.

- *Aortic Remodeling through 3-Year Follow-Up*

The AMDS is implanted in Zones 1-3 and may also extend into the distal section of the descending thoracic aorta (Zones 4 and 5). Radiographic assessment of aortic remodeling (defined as change in true lumen and false lumen diameter) was completed in Zones 1-6 (***Figure 3***). Aortic remodeling was assessed based on total aortic diameter (TAD), which was measured at distinct anatomical benchmarks: the innominate artery (IA), the left common carotid artery (LCCA), the left subclavian artery (LSA), and 2 cm distal to the LSA. Measurements were compared to pre-op measurements. A negative change indicates that the TAD decreased from pre-op. On average, there was a reduction in the aortic diameter just proximal to the edge of the IA at all post-operative visits, with only 1 case of increase > 5.0 mm (at 1-year), which was sustained through 3-years.

On average there was a small reduction and overall stability of the aortic diameter just proximal to the LCCA through 3-years. Aortic diameter growth ≥ 5.0 mm just proximal to

the LCCA was observed in 1 patient (5.0%) at discharge and 4 patients (19.0%) at 3-years. On average, the aortic diameter just proximal to the edge of the LSA artery was stable with < 5.0 mm of growth through 3-years.

Aortic diameter growth ≥ 5.0 mm just proximal to the LSA was observed in 1 patient (4.2%) at discharge and 4 patients (18.2%) at 3-years. On average, there was aortic diameter stability 2 cm distal to the LSA at early visits. True lumen expansion (≥ 5.0 mm) was demonstrated as early as pre-discharge, remaining stable and/or expanding through 3-years (*Error! Reference source not found.**21***).

Table 21. Change in True Lumen Diameter (mm) through 3-Years (DARTS I)

Zone	Pre-Op (n=41)	Pre-Discharge (n=32)		3 Months (n=31)		1-year (n=31)		3-years (n=29)	
	Mean (SD)	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline
1	19.2 (7.4)	30.4 (5.2)	12.2 (8.1)	31.8 (5.2)	13.8 (6.8)	31.9 (6.3)	14.6 (6.9)	31.6 (6.1)	13.8 (7.2)
2	19.4 (7.3)	29.9 (5.4)	10.8 (8.0)	28.6 (5.5)	11.2 (7.6)	29.9 (5.8)	13.1 (5.1)	30.4 (5.8)	13.3 (5.3)
3	18.5 (6.9)	23.8 (6.6)	5.1 (6.9)	23.7 (5.3)	6.2 (6.4)	24.9 (5.2)	7.3 (5.8)	25.2 (6.1)	8.2 (5.6)
4	18.1 (8.7)	23.6 (6.7)	5.4 (5.9)	23.2 (4.7)	5.9 (6.4)	24.6 (5.5)	7.6 (7.1)	24.8 (5.1)	7.2 (7.2)
5	14.3 (8.5)	24.7 (4.5)	9.5 (8.4)	23.1 (5.9)	8.4 (8.6)	23.3 (5.2)	9.4 (7.2)	23.2 (6.6)	9.9 (9.4)
6	13.7 (8.1)	16.8 (5.3)	2.6 (5.5)	15.4 (5.4)	0.5 (6.9)	15.7 (4.7)	0.6 (7.0)	16.7 (5.4)	2.9 (7.9)

Reported as mean (Standard Deviation or SD) diameter (mm).

Additionally, CT scan data was analyzed to evaluate the change in true lumen diameter at baseline and after AMDS implantation prior to discharge, 1-year, and 3-year nominal timepoints. Time was calculated for each subject based on the actual number of days between visits. The change in true-lumen diameter was modeled in aortic Zones 1-6 for pre-operative baseline to pre-discharge, (2) baseline to 1-year follow-up, and (3) baseline to 3-year follow-up, to evaluate the effect of AMDS on true lumen remodeling over time (***Figure 4***).

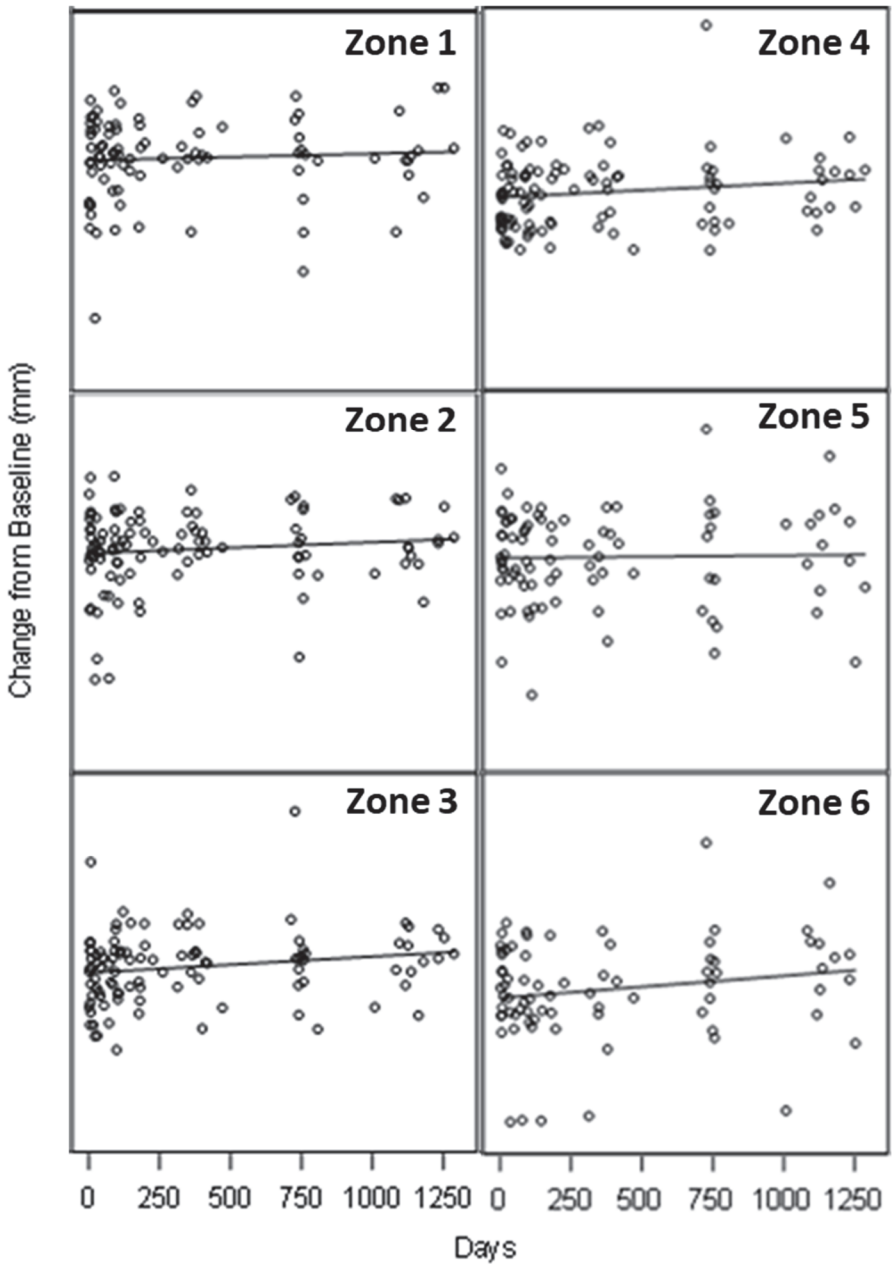

Figure 4. True Lumen diameter change from Baseline to 3-Year Follow-Up

The results indicate that the change in true lumen diameter after initial implantation of AMDS was not clinically meaningful or statistically significant in longer-term follow-up. An immediate increase in true lumen diameter was observed upon AMDS implantation with only a marginal mean increase in true lumen diameter (3.0mm) between pre-discharge and three years in Zones 1-3.

False lumen reduction (≤ 5.0 mm) was also demonstrated in most patients as early as patient discharge (***Table 22***). False lumen response in Zone 3 was variable and susceptible to continued false lumen flow if communications were present in the left subclavian artery or visceral segment near the infrarenal aorta.

Table 22. Change in False Lumen Diameter through 3 years (mm)

Zone	Pre-Op (n=41)	Pre-Discharge (n=32)		3 Months (n=31)		1-year (n=31)		3-years (n=29)	
	Mean (SD)	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline	Mean (SD)	Change from Baseline
1	20.1 (7.7)	8.1 (4.4)	-12.7 (8.5)	7.4 (4.8)	-13.8 (7.8)	7.6 (5.2)	-14.5 (8.0)	8.6 (6.5)	-13.3 (8.2)
2	16.6 (6.9)	6.6 (4.4)	-10.7 (7.6)	8.5 (5.3)	-9.8 (8.6)	7.7 (5.4)	-11.8 (5.0)	7.8 (6.4)	-11.9 (6.6)
3	15.3 (6.6)	11.9 (5.4)	-3.1 (6.8)	14.9 (6.6)	-1.3 (7.4)	14.4 (7.8)	-2.3 (7.0)	16.0 (11.1)	-1.2 (8.8)
4	16.8 (8.7)	12.9 (5.8)	-3.1 (5.9)	17.2 (7.6)	0.1 (6.4)	16.3 (7.8)	-1.4 (7.6)	17.4 (11.6)	-0.2 (9.8)
5	16.4 (9.0)	7.1 (5.1)	-7.4 (8.4)	12.6 (6.4)	-3.8 (8.3)	13.2 (6.9)	-3.1 (8.1)	15.8 (9.9)	-1.7 (10.9)
6	13.8 (8.5)	11.2 (6.6)	-1.9 (5.5)	14.8 (6.2)	2.2 (6.6)	15.6 (7.5)	3.6 (7.1)	16.1 (8.7)	2.4 (9.5)

Reported as mean (Standard Deviation or SD) diameter in mm.

Thrombosis of the false lumen (partial or complete, shown in ***Table 23***) was observed in the majority of the patients at discharge through 3-year follow-up.

Table 23. False Lumen Thrombosis Status through 3-Year Follow-Up (DARTS I)

Aortic Zone	False Lumen Thrombosis Status	Discharge		3-months		1-years		3-years	
		Total # of Patients	# (%)	Total # of Patients	# (%)	Total # of Patients	# (%)	Total # of Patients	# (%)
Zone 1	Completely Thrombosed	23	6 (26.1%)	25	5 (20.0%)	24	7 (29.2%)	21	7 (33.3%)
	Partially Thrombosed		8 (34.8%)		7 (28.0%)		5 (20.8%)		5 (23.8%)
	Patent		9 (39.1%)		13 (52.0%)		12 (50.0%)		9 (42.9%)
Zone 2	Completely Thrombosed	25	4 (16.0%)	26	6 (23.1%)	26	8 (30.8%)	23	8 (34.8%)
	Partially Thrombosed		10 (40.0%)		10 (38.5%)		7 (26.9%)		7 (30.4%)
	Patent		11 (44.0%)		10 (38.5%)		11 (42.3%)		8 (34.8%)
Zone 3	Completely Thrombosed	25	4 (16.0%)	26	3 (11.5%)	26	5 (19.2%)	24	6 (25.0%)
	Partially Thrombosed		12 (48.0%)		14 (53.8%)		11 (42.3%)		11 (45.8%)
	Patent		9 (36.0%)		9 (34.6%)		10 (38.5%)		7 (29.2%)

- *Assessment of Device Performance through 3-Year Follow-Up*

Radiographic secondary endpoints also included assessment of the device (***Table 24***). In total, 4 patients (9%) had evidence of device compression on ≥ 1 follow-up CTA; 1 patient (2%) had a twist noted, along with compression. Compression was defined by the Core Lab as 50% reduction in device diameter in comparison to diameters directly proximal or distal to the measurement area. In all cases of compression, there was no clinical sequelae reported. The Core Lab also evaluated for evidence of communications between the true lumen and false lumen throughout the aorta, specifically noting if DANE or d-SINE was present. There was no DANE or d-SINE noted in any discharge, 3-month, 1-year or 3-year CTAs.

Table 24. Device Assessment (DARTS I)

Device Characteristic	Discharge (n=26)	3-months (n=26)	1-year (n=29)	3-years (n=23)
Absence of stent fracture	100.0%	100.0%	100.0%	100.0%
Absence of stent compression	91.7%	90.9%	91.2%	89.7%
Absence of stent kinking	100.0%	100.0%	100.0%	100.0%
Absence of stent twist	97.2%	97.0%	97.1%	96.6%
Absence of Distal anastomotic new entry DANE tears	100.0%	100.0%	100.0%	100.0%
Absence of distal stent-induced new entry (d-SINE) tears	100.0%	100.0%	100.0%	100.0%

C. SUPPLEMENTAL CLINICAL DATA FOR THE AMDS

The following study provides additional real-world evidence on the safe use and performance of the AMDS.

The Berlin Heart Study published by Montagner et al. 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 patient anatomy (tortuous arch and proximal descending aorta), and narrowing diagnosed in a post-operative CT scan after uneventful intra- and perioperative course of treatment. Thirty-day follow-up data included 18% mortality, and operation-related new postoperative neurological deficit in 8% of patients. The 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.

XI. 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 14 of which none were full-time or part-time employees of the sponsor, with one investigator having 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: 0
- Significant payment of other sorts: 1
- 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. The information provided does not raise any questions about the reliability of the data.

Pediatric Extrapolation

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

XII. SAFETY AND PROBABLE BENEFIT ANALYSIS

A. Probable Benefit Conclusions

The PERSEVERE IDE study evaluated AMDS in the open surgical treatment of patients with acute DeBakey type I aortic dissection, with evidence of clinical and/or radiographic malperfusion.

Key device effectiveness findings from the data at ≤ 30-days include:

- 92/93 (98.9%) of procedures achieved technical success
    - 1 patient did not achieve technical success because while the majority of the device was implanted in the true lumen, the distal portion of the AMDS was inadvertently implanted into the false lumen through a secondary entry tear.
- Of 61 patients with adequate imaging to assess DANE, no patients had DANE.
- No patients had evidence of d-SINE, stent migration, stent fracture, stent twist, or stent kink.

The DARTS investigational study evaluated AMDS in the open surgical treatment of patients with acute DeBakey type I dissection, with and without evidence of clinical and/or radiographic malperfusion. Successful device deployment was achieved in 100% of patients.

No subjects experienced DANE through 3-years follow-up.

B. Safety Conclusions

Patient characteristics and safety outcomes from 198 patients treated with AMDS from the DARTS I, Berlin Heart Center, and PERSEVERE studies are summarized in ***Table 25***, as well as literature-based reference information, and demonstrate an acceptable benefit-risk profile for the AMDS.

Table 25. Comparison of Safety Outcomes of AMDS to Literature Reference Cohort

Outcome	DARTS I Study (Overall)[1]	DARTS I Study (MPS only)[2]	Berlin Heart Center Study[3]	PERSEVERE (MPS only)[4] *(Adjudicated)*	Literature-Based Reference Population (MPS only)[5]
Patient Characteristics					
Number of Patients	46	26	100	93	n/a
% Malperfusion	56.5%	100%	46%	100%	100%
% DeBakey Type I	100%	100%	100%	100%	70-100%
% Hemiarch Repair	97.8% (n=45)	100%	100%	100%	40-100%
Early Outcomes (≤ 30 Days)					
Intraoperative Mortality	2.2%	0%	4%	0%	12.3-36%
30 Day Mortality	13%	7.7%	18%	9.7%	13.4 – 43.7%
Disabling Stroke or Neurologic deficit	15.2%	23.0%	18%	7.5%	12.5 – 47.9%
Myocardial Infarction	0%	0%	0%	0%	6.8 – 16.1%
Renal Replacement Therapy/Dialysis	13.0%	19.2%	14%	18.3%	11 – 43%
Late Outcomes					
Mortality	21.7% (3-years)	15.4% (3-years)	n/a	n/a	16- 56.1% (3-years) 19.2% – 58.2% (5-years)

[1] DARTS I Clinical Report

[2] Bozso SJ N. J. et al. (2019) Single-Stage Management of Dynamic Malperfusion using a Novel Arch Remodeling Hybrid Graft

[3] Montagner M, et al. (2022) The arch remodelling stent for DeBakey I acute aortic dissection: experience with 100 implantations

[4] Data on file in interim analysis report (AMDS2101-IAR.003-C) and rates include events that are pending adjudication

[5] Reference Cohort: Bossone et al. 2002, Geirsson et al. 2007, Girdauskas et al. 2009, Pacini et al. 2013, Zindovic et al. 2019.

[6] Reference Cohort: Bing et al. 2014, Ergin et al 1994; Rylski et al 2017, Tamura et al. 2017.

The PRESERVE co-primary endpoints were met based upon the 30-day data. Safety and effectiveness will be evaluated at 1-year follow-up to support a future PMA.

The DARTS I Study longer-term data demonstrates that the AMDS is safe when implanted as directed in the Instructions for Use, with 22% all-cause mortality through 3-years (and no instance of early or late device-related mortality). Disabling stroke rates for all three AMDS studies were within the range reported in the literature for total stroke compared to literature reports (11.5 - 23% compared with 6.25 – 38.4%). There was no occurrence of myocardial infarction events in the three studies. Renal replacement therapy (RRT) required for patients with AMDS was in mid-range of RRT reported in the literature.

C. Probable Benefit-Risk Conclusions

The probable benefits of the device are also based on data [PERSEVERE Study, DARTS I Study, Berlin Heart Study] to support HDE approval as described above. The anticipated benefit to a patient implanted with the AMDS include reduced 30-day mortality in patients with preoperative malperfusion, complete closure of the intimal flap, positive aortic remodeling in the arch, and reduction of DANE tears and associated reoperations, when compared with patients treated with a standalone hemiarch repair procedure (per literature reports).

The probable risks of treatment with the AMDS are based on data collected in the clinical studies and real-world evidence are summarized above. These risks include mortality, disabling stroke, and myocardial infarction. The anticipated risks appear to be the same or lower than the risks associated with a standard open procedure based upon the currently available data and a comparison to the literature.

While risks have been identified with the use of the AMDS, the overall benefit-risk balance is positive in patients with acute DeBakey Type I aortic dissections with preoperative malperfusion. An additional factor for consideration in determining the probable risks and benefits of the AMDS include the absence of longer-term clinical follow-up data (e.g., complete 5-year follow-up data).

All-cause mortality and major adverse event rates are comparable to the results achieved the DARTS I and Berlin Heart Center studies and are within (or improved from) the range reported in the literature specifically for patients presenting with preoperative malperfusion. All data for the 30-day major adverse event rate in the PERSEVERE study was adjudicated.

In conclusion, for patients with acute DeBakey Type I aortic dissection, the probable benefits of the AMDS outweigh the probable risks.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the HDE for this device.

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and probable benefit of the AMDS when used in accordance with the indications for use. The pre-clinical testing performed per applicable guidance documents and international standards confirmed that the AMDS met is performance and design specifications.

The cumulative data from the PERSEVERE Pivotal Study, the DARTS I Study, and real-world evidence indicates that the AMDS is a safe option with probable benefit for treatment of acute DeBakey Type I aortic dissections in patients with malperfusion. Therefore, it is reasonable to conclude that the probable benefit to health from using the device for the target population outweighs the risk of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment when

used as indicated in accordance with the directions for use.

XIII. PANEL RECOMMENDATION

This HDE was not reviewed by an FDA Advisory Panel. The panel has previously reviewed similar implants. This HDE does not raise any unanticipated safety issues. Therefore, it was determined that this application need not be submitted to the advisory panel.

XIV. CDRH DECISION

CDRH has determined that, based on the data submitted in the HDE, the AMDS™ Hybrid Prosthesis will not expose patients to an unreasonable or significant risk of illness or injury and the probable benefit to health from using the device outweighs the risks of illness or injury. CDRH issued an approval order on December 4, 2024. The final clinical condition of approval cited in the approval order is described below.

Continued Follow-up of the IDE Study Subjects: This study is a prospective, single-arm, multi-center pivotal IDE study of the AMDS Hybrid Prosthesis. The study design includes the assessment of the AMDS for treatment of patients with Acute DeBakey I dissections with clinical or radiographic malperfusion. A total of 93 patients were included in the study. The remaining subjects will be followed annually for 5 years.

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 the device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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