SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Endovascular Graft

Device Trade Name: GORE® TAG® Thoracic Endoprosthesis

Device Procode: MIH

Applicant's Name and Address: W.L. Gore & Associates, Inc. (Gore)
3450 West Kiltie Lane
Flagstaff, Arizona 86001

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P040043/S051

Date of FDA Notice of Approval: September 10, 2013

Expedited: Not applicable

The GORE® TAG® Thoracic Endoprosthesis original PMA (P040043) was approved on March 23, 2005 for endovascular repair of aneurysms of the descending thoracic aorta (DTA). The indications for use were expanded to include the treatment of isolated lesion (excluding dissections) of the DTA in patients who have appropriate anatomy via P040043/S40 on January 13, 2012, based on the submission of data for the treatment of traumatic transections. The Summaries of Safety and Effectiveness Data (SSED) to support the original approval and the expanded indication are available on the CDRH website and are incorporated by reference here. The current supplement was submitted to further expand the indication for the GORE® TAG® Thoracic Endoprosthesis to include the treatment of all lesions of the DTA, including Type B dissections.

The data presented in this PMA supplement were for use of a modified device design, referred to as the conformable GORE® TAG® Thoracic Endoprosthesis (CTAG Device), as compared to the original PMA device; however, data from studies of this modified device were used to support approval of P040043/S39 and S40, for the treatment of aneurysms of the DTA and isolated lesions of the DTA (excluding dissections), respectively. Therefore, the modified device is currently marketed and this supplement was submitted to expand the indications for the device. The distinction is made because the conformable GORE® TAG® Thoracic Endoprosthesis is referred to as the CTAG Device throughout this

document in order to distinguish this new device design from previous iterations of the device.

When necessary, previous design iterations are referred to as the TAG Device for clarity. All versions of the device continue to be marketed as the GORE® TAG® Thoracic Endoprosthesis under PMA P040043.

It is important to point out that all previously submitted clinical data were considered with the acute complicated Type B aortic dissection data presented in S51 to support the indication for the CTAG Device to include treatment of all lesions of the DTA.

II. Indications for Use

The GORE® TAG® Thoracic Endoprosthesis is intended for endovascular repair of all lesions of the descending thoracic aorta, including:

- Isolated lesions in patients who have appropriate anatomy, including:
  - Adequate iliac / femoral access
  - Aortic inner diameter in the range of 16-42 mm
  - ≥ 20 mm non-aneurysmal aorta proximal and distal to the lesion
- Type B dissections in patients who have appropriate anatomy, including:
  - Adequate iliac / femoral access
  - ≥ 20 mm landing zone proximal to the primary entry tear; proximal extent of the landing zone must not be dissected
  - Diameter at proximal extent of proximal landing zone in the range of 16-42 mm

III. Contraindications

The GORE® TAG® Thoracic Endoprosthesis is contraindicated in:

- Patients with known sensitivities or allergies to the device materials (see **Table 1**)
- Patients who have a condition that threatens to infect the graft

IV. Warnings and Precautions

See Warnings and Precautions in the labeling (Instructions for Use).

The following information in this section is important in understanding the anatomical limitations described in the Indications for Use for the treatment of dissections:

When treating Type B dissections, the proximal extent of the intended proximal landing zone must not be dissected. For example, if the dissection or any hematoma in the proximal extent of the dissection extends up to the LSA, then coverage of the LSA would ensure the proximal end of the device lands in non-dissected tissue. Landing the proximal end of the device in dissected tissue could increase the risk of damage to the septum and could lead to new septal tears, aortic rupture, retrograde dissection, or other complications.

This clarification is needed because of the differences between neck limitations for aneurysms and landing zone limitations for dissections. Healthy neck lengths with the specified characteristics are needed in the treatment of aneurysms, but the landing zones do not need to be completely free of dissection. Additionally, the specific length of non-dissected aorta needed to avoid complications has not been demonstrated.

V. Device Description

The GORE® TAG® Thoracic Endoprosthesis provides endovascular repair of the DTA. The GORE® TAG® Thoracic Endoprosthesis may be used as a single device or in multiple device combination to accommodate the intended treatment site.

This device is a flexible, self expanding endoprosthesis that is constrained on the leading end of a delivery catheter. The device consists of the two parts, the endoprosthesis and the delivery system (**Figures 1** and **2**). Endoprosthesis sizes range in diameter 21 to 45mm and in length from 10 to 20cm. The compressed profile of these devices on a delivery catheter ranges from 18 to 24Fr.

The endoprosthesis consists of an ePTFE/FEP graft supported over its entire length by a nitinol wire frame (stent). A radiopaque gold band is embedded in the graft material at each end for device imaging. The stent is attached to the external surface of the graft by laminated ePTFE/FEP bonding tape. The proximal end of the endoprosthesis (stent graft) consists of exposed stent apices called partially uncovered stents, while the distal end of the stent is in line with the graft material. An ePTFE sealing cuff is attached over the stent to each end. For delivery, the endoprosthesis is mounted onto the delivery system. **Table 1** lists the materials in the GORE® TAG® Thoracic Endoprosthesis.

Table 1. GORE TAG Thoracic Endoprosthesis Materials

Materials
ePTFE (polytetrafluoroethylene)
FEP (fluoroethylpropylene)
Nitinol (Nickel, Titanium)
Gold

The delivery system consists of a catheter and a sewn deployment sleeve. The catheter is compatible with a 0.035" guidewire. Leading and trailing olives longitudinally restrain and protect the endoprosthesis during introduction. The leading olive contains a radiopaque marker band and a radiopaque soft tip to facilitate device placement. The trailing olive is constructed using a radiopaque material to facilitate device placement. The endoprosthesis is constrained by the sewn deployment sleeve and is mounted on the leading end of the catheter. Two leash lines attached to the olives and looped through the deployment line on either end of the constrained device prevent the device from rotating on the catheter. Pulling the deployment knob, which is attached to the deployment line system (not shown in **Figure 2**), unlaces the sleeve from the center out and allows the self expanding endoprosthesis to deploy. The sleeve is secured to the stent graft and remains implanted between the endoprosthesis and the vessel wall.

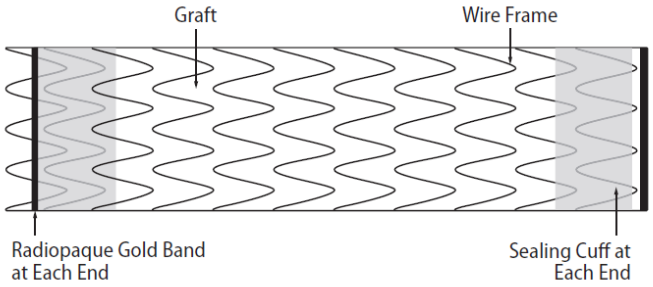

Figure 1. Conformable GORE® TAG® Thoracic Endoprosthesis

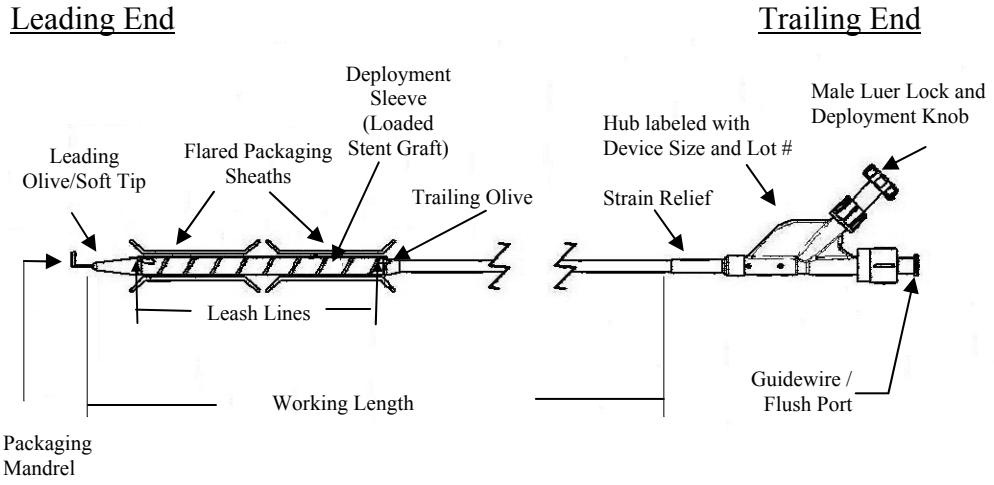

Figure 2. Delivery System

VI. Alternative Practices and Procedures

There are several other alternatives for treatment of the descending thoracic aorta including endovascular repair using another endovascular grafting system, surgical implantation of a synthetic graft within the aortic vessel, and medical management. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. Marketing History

Outside the United States, the GORE TAG Device has been marketed for nearly fifteen years for use in the endovascular repair of the descending thoracic aorta. The Conformable GORE TAG Device (CTAG Device) design iteration has been commercially distributed outside the US since 2009.

Besides the U.S., the CTAG Device is available in the following regions / countries: European Union, Canada, Australia, New Zealand, the Middle East, and Brazil.

The CTAG Device has not been withdrawn from the market for any reason.

VIII. Potential Adverse Effects of the Device on Health

Complications associated with the use of the CTAG Device may include, but are not limited to:

- Access, delivery and deployment events (e.g., access failure; deployment difficulties/failures; failure to deliver the stent graft; and insertion or removal difficulty)
- Adynamic ileus
- Allergic reaction (e.g., to contrast, anti-platelet therapy, stent graft material)
- Amputation
- Anesthetic complications
- Aortic expansion (e.g., aneurysm, false lumen, landing zone, lesion)
- Aortic rupture
- Angina
- Atelectasis/pneumonia
- Bleeding (procedural and post-treatment)
- Bowel (e.g., ileus, transient ischemia, infarction, necrosis)
- Branch vessel occlusion or obstruction
- Cardiac (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension or hypertension)
- Catheter breakage
- Change in mental status
- Coagulopathy
- Contrast toxicity
- Death
- Dissection, perforation, or rupture of the aortic vessel & surrounding vasculature
- Edema (e.g., leg)
- Embolism (micro and macro) with transient or permanent ischemia
- Endoleak
- Endoprosthesis: improper placement; incomplete deployment; migration; material failure; occlusion; infection; stent fracture; dilatation; perigraft flow
- Erectile dysfunction
- Erosion
- Excessive or inappropriate radiation exposure
- Femoral neuropathy
- Fever and localized inflammation
- Fistula (e.g., aortoeneteric, arteriovenous, aortoesophogeal, aortobronchial)
- Genitourinary (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- Hematoma
- Infarction
- Infection (e.g., aneurysm, device or access sites)
- Lymphocele/lymph fistula
- Myocardial infarction
- Neurological damage, local or systemic (e.g., stroke, paraplegia, paraparesis)
- Nerve injury
- Peripheral malperfusion or ischemia
- Persistent false lumen flow
- Post-implant syndrome
- Prosthesis dilatation/rupture
- Prosthetic thrombosis
- Pseudoaneurysm
- Pulmonary complications (e.g., pneumonia, respiratory failure)
- Pulmonary embolism
- Renal (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- Reoperation
- Restenosis
- Surgical conversion
- Thrombosis
- Transient ischemic attack
- Vascular spasm or vascular trauma (e.g., ilio-femoral vessel dissection, bleeding, rupture)
- Wound (e.g., infection, dehiscence)

IX. Summary of Preclinical Studies

The SSED containing the preclinical studies to support the indication for the previous TAG Device design is available on the CDRH website and is incorporated by reference here. Approval of the CTAG Device for the treatment of aneurysms included review of new preclinical studies. These data were reviewed under S39 and found adequate to support the broader indication of the treatment of isolated lesions under S40 and Type B dissection of the DTA under S51.

X. Summary of Primary Clinical Study

One primary clinical study (TAG 08-01) and one additional study (TAG 04-01) were conducted to support the expanded indication of all lesions of the DTA for the CTAG Device. Key characteristics of the clinical studies are provided in **Table 2**.

It should be noted that the safety of the CTAG Device for the treatment of all lesions of the DTA was not based on the TAG 08-01 (dissection) and TAG 04-01 (complex pathology including dissection) clinical studies alone, but rather on all the available data for the TAG and CTAG Devices to date, including data from TAG 08-03 (aneurysm) and TAG 08-02 (transection) that was reviewed under previous PMA supplements for the CTAG Device (P040043/S39 and P040043/S40, respectively). Further discussion of the supplementary information considered along with relevant factors regarding the patient populations covered under the indication of all lesions of the DTA will be provided subsequently along with clinical background information on Type B dissections.

Table 2. Clinical Studies

Clinical Study	Study Design	Objective	Number of Sites	Number of Subjects
TAG 08-01 (Acute Complicated Type B Dissection Pivotal Study)	Prospective, non-randomized, multi-center, single arm	Determine the safety and effectiveness of the CTAG Device for treatment of subjects with acute complicated Type B aortic dissection	Maximum of 50 sites approved for participation. A total of 26 sites enrolled subjects in the study cohort.	50 enrolled subjects 50 subjects included in primary endpoint analysis.
TAG 04-01 (DTA Complex Aortic Pathologies Feasibility Study)	Prospective, non-randomized, multi-center	Assess the initial feasibility of treating complex aortic pathologies with the TAG Device	14 sites	59 total (19 acute Type B dissection subjects)

TAG 08-01 – Acute Complicated Type B Aortic Dissection Pivotal Study Design

A. Study Design

The TAG 08-01 study (G090009) was a prospective, non-randomized, multi-center, single-arm evaluation, with the primary objective to assess the safety and effectiveness of the CTAG Device in subjects with acute complicated Type B aortic dissection. The primary safety endpoint was all cause mortality incidence through 30 days post-treatment. The primary effectiveness endpoint was exclusion of the primary entry tear at the 1 month follow-up visit (0 to 59 days post-treatment) as assessed by Core Lab analysis, and analyzed using descriptive statistics.

The primary hypothesis of the study was that all-cause mortality incidence through 30 days post-treatment met the performance goal of 25%. The study used Bayesian adaptive design methodology which allowed sample size to vary based on observed outcomes. A maximum of 50 investigative sites and up to 200 subjects were planned for participation in this study with a limit of 15 enrolled subjects per site. Patients were treated between 31 January 2010 and 10 January 2012. The database for this PMA/PMA supplement reflected data collected through 01 February 2013 and included 50 patients. There were 26 investigational sites.

Fifty (50) subjects treated with the CTAG Device for acute complicated Type B dissection were enrolled prior to the initial analysis. Data were to be analyzed after the initial cohort of 50 subjects completed 30 days of follow-up and, if needed, after each subsequent cohort of 25 subjects completed 30 days of follow-up. The three possible outcomes of each planned analysis were:

1) Termination of enrollment for success if the posterior probability using observed data was sufficient to meet the performance goal (99% probability or greater for 50 and 75 subject interim checks, 97.5% thereafter).
2) Continued accrual due to a reasonable predictive probability (10% or greater) that the performance goal could be met with the enrollment of additional subjects.
3) Termination of enrollment for futility if the predictive probability that the performance goal could be met with the enrollment of additional subjects was less than 10%.

Table 3 summarizes the sample size simulations and the probability required for determining study success at each analysis.

Table 3. Probability Required for Determining Study Success at Each Analysis

Analysis	Posterior Probability = Pr ($\theta < 0.25$ | data)	Decision	Posterior Predictive Probability of Study Success = Pr (success | data)	Decision
N=50	≥ 0.99	Stop (effective)	<0.10	Stop (futility)
N=75	≥ 0.99	Stop (effective)	<0.10	Stop (futility)
N=100	≥ 0.975	Stop (effective)	<0.10	Stop (futility)
N=125	≥ 0.975	Stop (effective)	<0.10	Stop (futility)
N=150	≥ 0.975	Stop (effective)	<0.10	Stop (futility)
N=175	≥ 0.975	Stop (effective)	<0.10	Stop (futility)
N=200	≥ 0.975	Meet Performance Goal		

Simulations of 100,000 clinical trials were conducted versus a range of values for the CTAG Device versus the performance goal value (0.25). The analysis strategy described controls the frequentist Type I error at 4.98% at the performance goal value of 0.25. These simulations took into account the potential premature termination of the study due to futility based on the predictive probability calculation at each point. These simulated calculations were made using exact results, since all of the distributions involved are solvable in closed form. A summary of the frequentist power calculation is provided in **Table 4**.

Table 4. Simulated Power under Planned Analysis Scenario vs Performance Goal

CTAG Device 30 Day Mortality	0.25 (Performance Goal)
0.1	100
0.11	100
0.12	99
0.13	98
0.14	96
0.15	92
0.16	85
0.17	76
0.18	65
0.19	53
0.2	41

Note: Entries represent percent of simulated trials which concluded that the CTAG Device cohort meets the performance goal (0.25) given the proportions listed.

Three separate external evaluation groups independently reviewed data for this study. They included a Data and Safety Monitoring Board (DSMB), a Clinical Events Committee (CEC), and an independent imaging Core Lab.

The DSMB was utilized to review all study data. After review of study data, the DSMB made recommendations to the sponsor. Recommendations could have included modifying the study, stopping the study, or continuing the study without modification. The DSMB made no recommendations to modify or discontinue the TAG 08-01 study.

The CEC was utilized to review adverse event data to ensure consistent and accurate AE and death reporting and classification. All major adverse events and major device events were adjudicated for accurate reporting of the adverse event severity, relationship to aortic rupture or malperfusion and relationship to the device or endovascular procedure through 1 year post-procedure. Each event was independently reviewed by three CEC members or by full panel review in cases of disagreement. A subcommittee of the CEC, comprised of two neurologists, was formed during the conduct of the study to evaluate several factors associated with the general event of stroke.

The imaging Core Lab, AortaCore, located at the University of Wisconsin-Madison was utilized to provide a separate review of CT and radiograph films collected for the study. In addition, the primary effectiveness endpoint result was based on the Core Lab assessment.

1. Clinical Inclusion and Exclusion Criteria

Subjects were screened and eligibility for enrollment into the study was determined by the Investigator. Pre-treatment evaluation included a contrast enhanced spiral computed tomographic angiography (CTA) of the chest, abdomen, and pelvis to assess aortic morphology and vascular characteristics. A physical exam including assessment for inclusion/exclusion criteria, medical history, subject risk status using Society of Vascular Surgery (SVS) and the American Society of Anesthesiology (ASA) guidelines, blood pressure, concomitant medications and serum creatinine concentration was performed for each subject.

Enrollment in the study was limited to patients who met the following inclusion criteria:

1) Presence of acute complicated Type B aortic dissection:
   - Dissection is acute
     Time from symptom onset to dissection diagnosis ≤14 days
   - Dissection is complicated
     Subject must present with at least one of the following:

- Rupture in the setting of an aortic dissection defined as hemorrhage outside of the aortic boundaries which is noted by CT scan (hemorrhage must be differentiated from reactive effusions by the investigator, or if equivocal, having elevated Hounsefield units as determined by the radiologist)
- Clinical evidence of malperfusion, in the setting of an aortic dissection, defined as:
  - Clinical or radiographic evidence of visceral hypoperfusion
  - Clinical or radiographic evidence of renal hypoperfusion
  - Clinical or radiographic evidence of lower extremity hypoperfusion
  - Clinical or radiographic evidence of spinal cord hypoperfusion

- Dissection is Type B
  Entire dissection is distal to the left subclavian artery
- Primary Treatment Indication is Class 1 Aortic Dissection
  Classical aortic dissection with intimal flap between true and false lumen with double barrel flow in thoracic aorta
- Subjects with multiple entry tears are allowed to be enrolled in the study

2) Age 18 to 80 years
3) Primary treatment is endovascular treatment with the CTAG Device. Adjunctive treatments may include left subclavian artery revascularization, percutaneous fenestration, aortic stenting, peripheral vessel stenting, surgical fenestration, and/or peripheral artery bypass
4) Proximal landing zone characteristics include:
   - Proximal extent of intended proximal landing zone cannot be dissected
   - Length $\geq$ 2.0 cm proximal to the primary entry tear
   - Trans-aortic diameter at proximal extent of intended landing zone between 16-42 mm (diameter assessed by flow lumen and thrombus, if present; calcium excluded)
   - Cannot be aneurysmal, heavily calcified, or have excessive intraluminal thrombus
   - Must be native aorta
   - May include left subclavian artery, if necessary
5) Subject is capable of complying with protocol requirements, including follow-up
6) Informed Consent Form is signed by subject or legal representative

Patients were not permitted to enroll in the study if they met any of the following exclusion criteria:

1) Primary treatment indication is Class 2-5 aortic dissection (intramural hematoma, limited dissection, penetrating atherosclerotic ulcer, iatrogenic dissection, traumatic dissection)
2) Concomitant aneurysm/disease of the ascending aorta, aortic arch, or abdominal aorta requiring repair (dissection extension into the abdominal aorta is acceptable)
3) Prior repair of DTA
4) Infected aorta
5) Subject has a systemic infection and may be at increased risk of endovascular graft infection
6) Persistent refractory shock (systolic blood pressure <90 mm Hg)
7) Bowel necrosis (bowel necrosis characterized by direct observation with surgical exploration, or elevated serum lactate level and CT findings of portal venous gas, free intra-abdominal gas, pneumatosis intramural gas, and poor mucosal enhancement of thickened bowel wall)
8) Renal failure, defined as baseline creatinine ≥ 2.5 mg/dl
9) ASA risk classification = V (moribund patient not expected to live 24 hours with or without operation)
10) Pregnant female
11) Major surgery within 30 days of treatment (other than left subclavian artery bypass or transposition)
12) Degenerative connective tissue disease (e.g., Marfan or Ehler-Danlos Syndrome)
13) Treatment in another drug or medical device study within 1 year of study enrollment
14) History of stimulant abuse (e.g., cocaine or amphetamine) within 1 year of treatment
15) Tortuous or stenotic iliac and/or femoral arteries and the inability to use a conduit for vascular access
16) Planned coverage of left carotid or celiac arteries with the CTAG Device
17) The planned endovascular procedure involves alterations to the CTAG Device
18) Subject has known sensitivities or allergies to the device materials

2. Follow-up Schedule

Preoperatively, subjects were required to have a spiral CT, physical examination, and serum creatinine concentration measurement to assess their eligibility for participation in the study.

The subject schedule of follow-up is described in **Table 5**. This included returning for follow-up visits at 1 month, 6 months, 1 year and annually thereafter

through 5 years. Follow-up procedures required a physical examination, four view chest X-ray, spiral CT of the chest, abdomen, and pelvis (contrast and non-contrast), and assessment for adverse events and device events.

Table 6 provides a description of the pre-operative and post-operative evaluations and assessments that were performed to assess subject eligibility and effectiveness endpoints. Adverse events and complications were recorded at all visits.

Table 5. TAG 08-01 Subject Schedule of Events

Diagnostic Test	Pre-treatment	Treatment	Discharge	1 month	6 months	Annually for up to 5 years
Physical examination	X		X	X	X	X
Creatinine Concentration	X					
Spiral CT	X		X	X	X	X
Angiogram		X				
Chest x-ray			X	X	X	X

Table 6. Description of Pre-Operative & Post-Operative Evaluations & Assessments

Timepoint	Evaluative point	Description	Evaluative Tools	Assessment Point
Pre-Operative	Anatomic Eligibility	Patient Eligibility	CT Scan with/without contrast	Candidacy for endovascular repair
	Medical Eligibility	Patient Eligibility	Physical Exam	Verify study inclusion/exclusion criteria including the presence of an acute, complicated dissection
	Renal Function	Patient Eligibility	Serum Creatinine	Verify study inclusion/exclusion criteria and potential for contrast-enhanced follow-up evaluations
Post-Operative	Vital Status	Primary Safety Endpoint (Evaluated at 30 Days)	Any	Verify that the subject was alive at 30 days post-procedure
	Primary Entry Tear Exclusion	Primary Effectiveness Endpoint (Evaluated at 1 Month)	Contrast-enhanced CT scan	False lumen is not perfused through the primary entry tear as visualized by contrast dye. Core Lab evaluated.
	False Lumen Thrombosis	Secondary Effectiveness Endpoint (Evaluated at each follow-up visit)	Contrast-enhanced CT scan	Characterization of false lumen status adjacent and distal to the stent graft. Core Lab evaluated.

Timepoint	Evaluative point	Description	Evaluative Tools	Assessment Point
	Dissection-Based Interventions	Secondary Effectiveness Endpoint (Evaluated at each follow-up visit)	Contrast-enhanced CT scan, Physical Exam	Identification of surgical/endovascular procedures performed and associated with underlying disease process (malperfusion or rupture). Events occurring within one year of procedure are adjudicated by CEC.
	Aortic Rupture	Secondary Effectiveness Endpoint (Evaluated at each follow-up visit)	Contrast-enhanced CT scan, Physical Exam, Autopsy	Freedom from aortic rupture.

3. Clinical Endpoints

With regards to safety, the primary hypothesis of the study was that all-cause mortality incidence through 30 days post-treatment met the performance goal of 25%. The performance goal was justified based on historical data, including the SVS Master File[1], open and endovascular literature, and the International Registry of Acute Aortic Dissection (IRAD) data available at the time the protocol was developed.

With regards to effectiveness, the primary effectiveness endpoint of primary entry tear exclusion was evaluated for subjects completing a 1 month visit with CT or MR imaging provided to the Core Lab.

Secondary effectiveness endpoints were evaluated at 1 month, 6 months and 12 months, and included the following:

- False Lumen Thrombosis (evaluated by Core Lab analysis). This was evaluated at each follow-up visit and categorized as follows:
  - Incomplete thrombosis – presence of blood flow in any portion of the false lumen parallel to the stent graft, excluding the distal 2cm.
  - Complete thrombosis – absence of blood flow in any portion of the false lumen parallel to the stent graft, excluding the distal 2cm.
  - No false lumen thrombosis - presence of blood flow throughout the entire false lumen within the descending thoracic aorta parallel to the stent graft.
- Additional Dissection Based Intervention Rate (reported by site) defined as interventions that were related to malperfusion or aortic rupture.
- Aortic Rupture (reported by the site).

Although the primary and secondary effectiveness endpoints were not hypothesis driven, they are clinically meaningful in assessing the effectiveness of treatment of acute complicated Type B dissections. These effectiveness endpoints were qualitatively compared to historical endovascular literature and were found to be comparable.

With regard to success/failure criteria, the overall TAG 08-01 study was considered successful if the primary safety endpoint result met the pre-specified performance goal. No individual subject success/failure criteria were defined in the protocol.

B. Accountability of PMA Cohort

Subjects were screened and enrolled per the procedures per the protocol**.** A total of 170 patients were screened for eligibility in the TAG 08-01 study; 120 subjects were excluded from study participation (**Figure 3**). The reasons for screen failure included:

- Anatomic considerations due to proximal landing zone characteristics per inclusion criterion 4 or inadequate access per exclusion criterion 15 (n=28)
- Subject not presenting with an acute complicated Type B dissection as defined in the protocol per inclusion criterion 1 or exclusion criterion 1 (n=47)
- Concomitant disease/disease process per exclusion criteria 2-8 or 12 (n=22)
- Primary treatment plan was not placement of a thoracic stent graft per inclusion criterion 3 or exclusion criteria 16-17 (n=12)
- Age requirements per inclusion criterion 2 (n=2)
- Drug abuse/study compliance per inclusion criterion 5 or exclusion criterion 14 (n=5)
- Major surgery within 30 days per exclusion criterion 11 (n=2)
- Inability to obtain informed consent per inclusion criterion 6 (n=2)

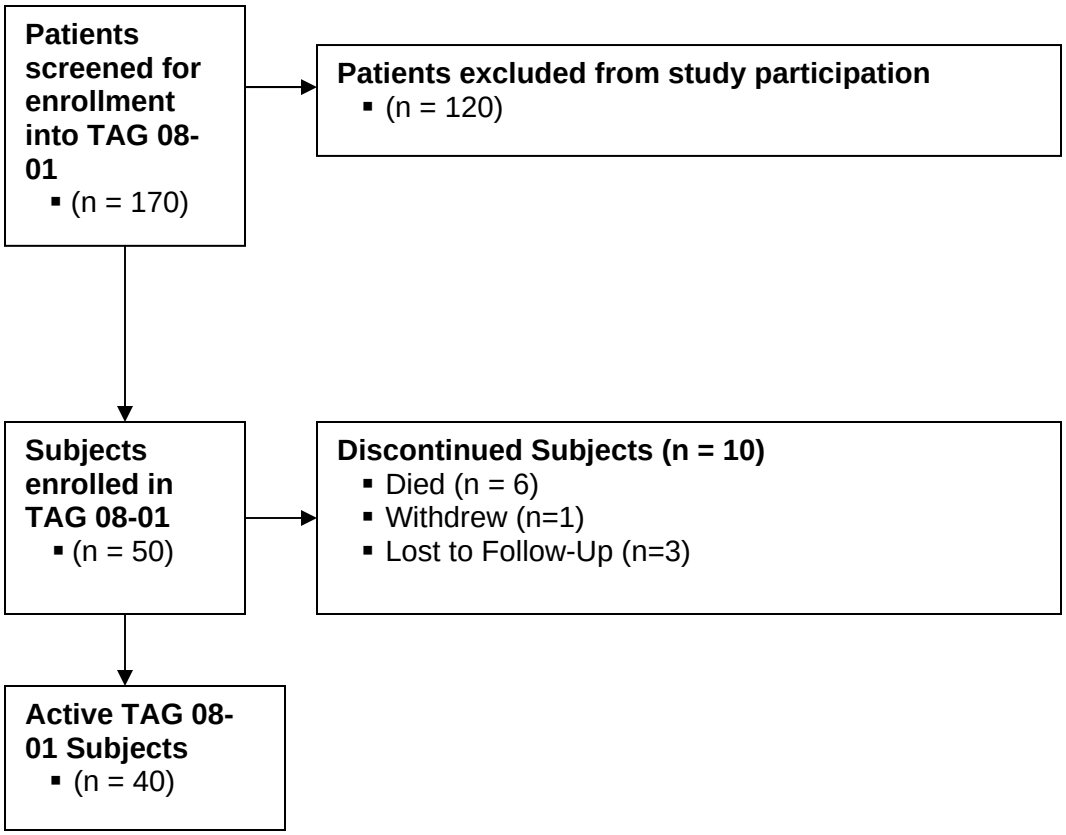

Figure 3. TAG 08-01 Study Subject Disposition Flowchart

A total of 50 subjects were enrolled at 26 investigative sites from January 2010 to January 2012. All enrolled subjects underwent endovascular repair with the CTAG Device to treat acute complicated Type B aortic dissection. Subjects enrolled in TAG 08-01 were required to return for follow-up visits as described in **Table 5**.

Table 7 summarizes compliance with protocol required visits and imaging along with discontinuation from the study. All subject visits through 12 months are complete. Subjects remain in follow-up therefore data beyond 12 months are incomplete.

Table 7. Subject Disposition and Compliance by Study Interval

		Follow-up Compliance			Events Prior to Next Interval		
Study Period	**Eligible for follow-up**	**Subjects with Visit in Window**	**CT Scan performed[1]**	**X-Ray performed[1]**	**Death[1]**	**Discontinued[1]**	**Not Due for Next F/U[1]**
Procedure	50	-	-	-	2 (4.0%)	0 (0.0%)	0 (0.0%)
Post-Procedure	48	-	-	-	2 (4.2%)	1 (2.1%)	0 (0.0%)
1 Month	45	45 (100.0%)	41 (91.1%)	39 (86.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
6 Months	45	41 (91.1%)	38 (84.4%)	34 (75.6%)	2 (4.4%)	0 (0.0%)	0 (0.0%)
12 Months	43	39 (90.7%)	38 (88.4%)	35 (81.4%)	0 (0.0%)	2 (4.7%)	8 (18.6%)
24 Months	33	20 (60.6%)	20 (60.6%)	16 (48.5%)	0 (0.0%)	1 (3.0%)	23 (69.7%)
36 Months	9	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (100.0%)
48 Months	0	-	-	-	-	-	-
60 Months	0	-	-	-	-	-	-

Study period definitions: Procedure(0-0 days) Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)

[1] Percentages are based on number of subjects in visit window. Compliance is based on site reported imaging assessments.

C. Study Population Demographics and Baseline Parameters

Baseline assessments of TAG 08-01 study subjects include demographics, presenting dissection characteristics, risk factor evaluations, medical history, and radiological aortic assessment.

Table 8 provides a summary of demographic data. A majority of subjects (74%) were male. Caucasians comprised 56.0% of the cohort. Median subject age was 57.5 years (range: 31-83 years).

Subject medical history is presented in **Table 9**. Most commonly noted at the pre-treatment visit were hypertension, history of smoking, and hypercholesterolemia.

Table 8. Subject Demographics

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Gender	
Male	37 (74.0%)
Female	13 (26.0%)
Ethnicity	
Not Hispanic or Latino	46 (92.0%)
Hispanic or Latino	4 (8.0%)
Race	
White or Caucasian	28 (56.0%)
Black or African American	17 (34.0%)
Asian / Oriental	1 (2.0%)
American Indian or Alaskan Native	1 (2.0%)
Native Hawaiian or Other Pacific Islander	0 (0.0%)
Middle Eastern	0 (0.0%)
Other	3 (6.0%)
Unknown	0 (0.0%)
Age (yrs)	
n	50
Mean (Std Dev)	57.1 (11.6)
Median	57.5
Range	(31.0, 83.0)
Weight (kg)	
n	50
Mean (Std Dev)	97.4 (23.5)
Median	94.3
Range	(58.5, 148.0)
Height (cm)	
n	49
Mean (Std Dev)	173.5 (10.2)
Median	175.0
Range	(152.4, 201.0)

Table 9. Subject Medical History

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Hypertension	47 (94.0%)
Cigarette Smoking	27 (54.0%)
Hypercholesterolemia	16 (32.0%)
Renal Insufficiency	11 (22.0%)
COPD	10 (20.0%)
Cardiac Arrhythmia	10 (20.0%)
Diabetes Mellitus	9 (18.0%)
CAD	7 (14.0%)
Myocardial Infarction	6 (12.0%)
Cancer	5 (10.0%)
Peripheral Vascular Disease	5 (10.0%)
Stroke	5 (10.0%)
CHF	3 (6.0%)
CABG	2 (4.0%)
Cardiac Surgery	2 (4.0%)
Carotid Disease	2 (4.0%)
Prior Aortic Dissection	2 (4.0%)
Abdominal Aortic Aneurysm	1 (2.0%)
Paraplegia	1 (2.0%)
TIA	1 (2.0%)
Abdominal Aortic Surgery	0 (0.0%)
Aortic Valve Replacement	0 (0.0%)
Thoracotomy	0 (0.0%)

Since the Society for Vascular Surgery Master File (SVS MF) was used in developing the performance goal, the baseline characteristics (demographics and medical history) were compared to investigate potential differences between the datasets as shown in **Table 10**. Although some differences were noted in the comparison of the SVS MF and the TAG 08-01 study patient population such as smoking status, renal malperfusion, lower extremity malperfusion and ASA classification, the majority of the baseline characteristics were comparable between the two datasets. Therefore, the overall patient population from this PMA study is comparable to the patient population from the SVS MF and the use of the SVS MF in evaluating study results is reasonable.

Table 10. Baseline Characteristics Comparison

Variable	Level	TAG 08-01 n=50	SVS Master File n=85	p-value[1]
Demographics	N (%) unless otherwise indicated			
Gender	**Male**	37 (74.0)	62 (72.9)	1.00
	Female	13 (26.0)	23 (27.1)	
Age in years, mean (sd)		57.1 (11.6)	58.8 (15.4)	0.51
Race	**White/Caucasian**	28 (56.0)	45 (52.9)	0.94
	Black/African American	17 (34.0)	23 (27.1)	
	American Indian/Alaskan Native	1 (2.0)	1 (1.2)	
	Native Hawaiian/Pacific Islander	0 (0.0)	1 (1.2)	
	Asian	1 (2.0)	3 (3.5)	
Hispanic Ethnicity	**Hispanic**	4 (8.0)	12 (14.1)	0.41
	Non-Hispanic	46 (92.0)	72 (84.7)	
Medical History				
Diabetes	**Yes**	9 (18.0)	11 (12.9)	0.46
Cancer	**Yes**	5 (10.0)	8 (9.4)	1.00
Cerebrovascular Event	**Yes**	5 (10.0)	3 (3.5)	0.15
TIA	**Yes**	1 (2.0)	0 (0.0)	0.37
COPD	**Yes**	10 (20.0)	9 (10.6)	0.20
CHF	**Yes**	3 (6.0)	9 (10.6)	0.53
HTN	**Yes**	47 (94.0)	71 (83.5)	0.11
MI	**Yes**	6 (12.0)	10 (11.8)	1.00
Arrhythmia	**Yes**	10 (20.0)	10 (11.8)	0.22
Smoking Status[2]	**Current**	25 (50.0)	27 (31.8)	<0.0001
	Prior History	2 (4.0)	31 (36.5)	
	Never Smoked	23 (46.0)	25 (29.4)	
Diagnosis				
Rupture	**Yes**	11 (22.0)	27 (31.8)	0.24
Malperfusion	**Yes**	41 (82.0)	61 (71.8)	0.22
Visceral Malperfusion	**Yes**	15 (30.0)	12 (14.1)	0.26
Renal Malperfusion	**Yes**	30 (60.0)	22 (25.9)	0.012
Lower Extremity Malperfusion	**Yes**	18 (36.0)	34 (40.0)	0.056*
Spinal Malperfusion	**Yes**	3 (6.0)	2 (2.4)	0.66
ASA Grade	**1**	2 (4.0)	0 (0.0)	0.0038
	2	2 (4.0)	2 (2.4)	
	3	20 (40.0)	19 (22.4)	
	4	26 (52.0)	55 (64.7)	
	5	0 (0.0)	9 (10.6)	

[1] p-values are based on Fisher's exact test for categorical variables and two-sample t-tests for continuous variables.

[2] TAG 08-01 smoking categories were condensed to match with closest SVS MF category.

*In SVS group there were 24 missing values for lower extremity malperfusion, for a rate of 55.7% among the nonmissing, which is reflected in the p-value.

Table 11 summarizes pre-treatment risk using several criteria including ASA and New York Heart Association (NYHA) Functional Classification. Most subjects were classified as ASA IV, defined as severe systemic disease that is a constant threat to life. Few subjects were enrolled with notable cardiac dysfunction based on the NYHA classification.

Table 12 summarizes details of the presentation of the aortic dissection, including symptoms, days from symptom onset to diagnosis, complications of dissection and malperfused vascular beds in the subset of subjects enrolled with malperfusion syndrome. Back, chest, and abdominal pain were the most commonly reported symptoms. All subjects were diagnosed with aortic dissection within 14 days of symptom onset. Thirty nine (39) subjects presented with malperfusion (78%), 9 with rupture (18%) and 2 with both malperfusion and rupture. Subjects presenting with malperfusion may have more than one vascular bed/organ malperfused. Renal malperfusion was present in 30 subjects (73%), followed by lower limb malperfusion in 18 (44%) and visceral malperfusion in 15 (37%). Spinal cord malperfusion was seen in 3 subjects (7%). The majority of dissections extended down to the iliac arteries (60%). **Table 13** summarizes the observed malperfusion combinations.

Subjects underwent pre-treatment imaging to assess aortic morphology and whether appropriate anatomy existed for inclusion in the TAG 08-01 study (**Table 14**). Criteria for enrollment included proximal landing zone length $\geq$ 2.0 cm from the primary entry tear to the left common carotid and proximal aortic diameter measured within the range of 16-42 mm.

Table 11. Pre-Treatment Risk Summary

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
ASA Classification	
I	2 (4.0%)
II	2 (4.0%)
III	20 (40.0%)
IV	26 (52.0%)
V	0 (0.0%)
NYHA Classification	
I	11 (22.0%)
II	6 (12.0%)
III	1 (2.0%)
IV	0 (0.0%)
No Cardiac Disease	32 (64.0%)

Table 12. Presenting Dissection Characteristics

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Symptoms of Aortic Dissection	
Back Pain	40 (80.0%)
Chest Pain	33 (66.0%)
Abdominal Pain	25 (50.0%)
Peripheral Pulse Deficit	15 (30.0%)
Leg Pain	7 (14.0%)
Hypotension	3 (6.0%)
Syncope	2 (4.0%)
Dysphonia	1 (2.0%)
Dysphagia	0 (0.0%)
Hemoptysis	0 (0.0%)
Days from Symptom Onset to Diagnosis	
n	50
Mean (Std Dev)	1.2 (1.8)
Median	0.4
Range	(0.0, 7.3)
Days from Symptom Onset to Diagnosis	
<7 Days	49 (98.0%)
7-14 Days	1 (2.0%)
>14 Days	0 (0.0%)
Known Distal Extent of Dissection (Core Lab)	
DTA	5 (10.0%)
Celiac	4 (8.0%)
SMA	1 (2.0%)
Renals	5 (10.0%)
IMA	5 (10.0%)
Iliacs	30 (60.0%)
Complications of Dissection	
Malperfusion	39 (78.0%)
Rupture	9 (18.0%)
Malperfusion and Rupture	2 (4.0%)
Subjects with Malperfusion[1]	41
Visceral Malperfusion	15 (36.6%)
Renal Malperfusion	30 (73.2%)
Lower Extremity Malperfusion	18 (43.9%)
Spinal Cord Malperfusion	3 (7.3%)

[1] Percentages below this heading use this value as the denominator.

Table 13. Observed Malperfusion Combinations

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Subjects with Malperfusion	41
Presenting Malperfused Vascular Beds	
Renal Only	12(29.3%)
Lower Extremity Only	7(17.1%)
Visceral and Renal	7(17.1%)
Renal and Lower Extremity	5(12.2%)
Visceral Only	3(7.3%)
Visceral, Renal, and Lower Extremity	3(7.3%)
Renal and Spinal Cord	1(2.4%)
Renal, Lower Extremity, and Spinal Cord	1(2.4%)
Visceral and Lower Extremity	1(2.4%)
Visceral, Renal, Lower Extremity, and Spinal Cord	1(2.4%)
Lower Extremity and Spinal Cord	0(0.0%)
Spinal Cord Only	0(0.0%)
Visceral and Spinal Cord	0(0.0%)
Visceral, Lower Extremity, and Spinal Cord	0(0.0%)
Visceral, Renal, and Spinal Cord	0(0.0%)

Table 14. Pre-Treatment Imaging Characteristics (Site Reported)

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Aortic Diameter at Proximal Implantation Site (mm)	
n	49
Mean (Std Dev)	30.8 (3.8)
Median	31.0
Range	(24.0, 42.0)
Maximum True Lumen Diameter (mm)	
n	50
Mean (Std Dev)	24.5 (8.9)
Median	23.5
Range	(8.0, 58.0)
Minimum True Lumen Diameter (mm)	
n	50
Mean (Std Dev)	11.6 (8.9)
Median	10.0
Range	(0.0, 46.0)
Maximum False Lumen Diameter (mm)	
n	50
Mean (Std Dev)	28.0 (8.5)
Median	28.5
Range	(12.0, 45.0)
Maximum Transverse Diameter (mm)	
n	50

	TAG 08-01 Cohort
Mean (Std Dev)	40.2 (8.1)
Median	38.5
Range	(28.0, 65.0)
Proximal Neck Length (Primary Entry Tear-LCCA) (cm)	
n	49
Mean (Std Dev)	4.9 (3.8)
Median	3.5
Range	(2.0, 16.3)
Dissection Length (cm)	
n	47
Mean (Std Dev)	35.1 (15.7)
Median	38.3
Range	(3.9, 66.0)
Distal Re-entry Tears	
No	18 (36.0%)
Yes	31 (62.0%)
Missing	1 (2.0%)
Left Common Iliac Diameter (mm)	
n	49
Mean (Std Dev)	14.6 (3.7)
Median	14.0
Range	(7.0, 27.0)
Left External Iliac Diameter (mm)	
n	49
Mean (Std Dev)	9.6 (2.1)
Median	10.0
Range	(0.0, 13.0)
Right Common Iliac Diameter (mm)	
n	49
Mean (Std Dev)	13.6 (3.4)
Median	14.0
Range	(4.0, 25.0)
Right External Iliac Diameter (mm)	
n	49
Mean (Std Dev)	9.9 (2.1)
Median	10.0
Range	(0.0, 15.0)

Treatment Details

A summary of treatment characteristics is provided in **Table 15**. Included are general characteristics on access method and site, anesthesia, and adjunctive techniques to prevent paraplegia. All procedures (100%) were performed under general anesthesia and vascular access was gained via the femoral artery in 92% (cut-down in 74%, percutaneous in 20% and conduit in 6%). Adjunctive techniques to prevent paraplegia were performed (CSF drainage in 64.7% and induced hypertension in 5.9%). The left subclavian artery (LSA) was covered completely in 54% of subjects and partially covered in 18% of subjects. LSA bypass was performed in 14% and transposition in 4%. Proximal device implantation occurred in Zone 2 for 72% of subjects and Zone 3 / 4 for 28%.

Device use data are provided in **Table 16** and **Table 17**. The majority of cases were treated with one device with a significant portion of Investigators also electing to use a second device. The mean device use per subject was 1.5 devices. Generally, longer devices were used with 10cm length devices only accounting for 15% of total devices used. The most common device diameter was 34mm which is roughly in the middle of the CTAG Device diameter portfolio.

Device usage in the study was consistent with the expectations of use to treat aortic dissection. The treatment goal is exclusion of the primary entry which usually can be accomplished with one device. Additional implanted devices can constitute a surgeon's decision to extend the treatment zone to exert more longitudinal pressure on the false lumen, cover a significant fenestration in the aortic septum, or part of a conservative approach in an aortic rupture. The distribution of device diameters may be characteristic of middle-age subjects who are starting to exhibit underlying vascular disease and whose aorta has not gone through a degenerative process as much as the typical aneurysm patient.

The TAG 08-01 study procedural outcomes are displayed in **Table 18**. All subjects survived the endovascular procedure. The median case time was 168 minutes and the median blood loss was 200mL. The median hospital stay after endovascular treatment with the CTAG Device was 10 days (range 0-41 days). All subjects had ICU stay and with a median ICU stay was 4.8 days. The hospital survival was 92% as noted in **Table 23**. Fifty-two percent (52%) of subjects underwent an adjunctive procedure at the index procedure with placement of a peripheral stent being the most common procedure. These adjunctive procedures were intended to address the complications of the aortic dissection itself and the presenting symptoms, rather than related to the placement of the device.

Table 15. Summary of Treatment Characteristics

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
LSA Procedure	
None	41 (82.0%)
Transposed	2 (4.0%)
Bypassed	7 (14.0%)
Access Method	
Percutaneous	10 (20.0%)
Cut-Down	37 (74.0%)
Cut-Down and Conduit	3 (6.0%)
Access Site	
Femoral Artery	46 (92.0%)
Iliac Artery	4 (8.0%)
Infrarenal Aorta	0 (0.0%)
Anesthesia Method	
General	50 (100.0%)
Regional	0 (0.0%)
Local	0 (0.0%)
Adjunctive Techniques to Prevent Paraplegia[1]	17 (34.0%)
CSF Drainage	11 (64.7%)
Induced Hypertension	1 (5.9%)
Other	5 (29.4%)
Proximal Implantation Zone	
Zone 2	36 (72.0%)
Zone 3 / Zone 4	14 (28.0%)
LSA Coverage	
Complete	27 (54.0%)
Partial	9 (18.0%)
None	14 (28.0%)

[1] This count used as denominator for percentages under this heading.

Table 16. Implanted Device Characteristics[1]

			Initial Procedure	
Proximal Diameter (mm)	**Distal Diameter (mm)**	**Length (cm)**	**Subjects[2] (N=50) n (%)**	**Devices[3] (N=74) n (%)**
28	28	10	2 (4.0%)	2 (2.7%)
28	28	15	3 (6.0%)	3 (4.1%)
31	31	10	2 (4.0%)	2 (2.7%)
31	31	15	12 (24.0%)	14 (18.9%)
34	34	10	2 (4.0%)	2 (2.7%)
34	34	15	6 (12.0%)	6 (8.1%)
34	34	20	17 (34.0%)	17 (23.0%)
37	37	10	3 (6.0%)	3 (4.1%)
37	37	15	6 (12.0%)	6 (8.1%)
37	37	20	5 (10.0%)	5 (6.8%)
40	40	10	2 (4.0%)	2 (2.7%)
40	40	15	6 (12.0%)	6 (8.1%)
40	40	20	4 (8.0%)	4 (5.4%)
45	45	20	2 (4.0%)	2 (2.7%)

[1]Five GORE TAG Device sizes were not implanted as part of this study. Those sizes are the 21mm x 21mm x 10cm, 26mm x 21mm x 10cm, 26mm x 26mm x 10cm, 31mm x 26mm x 10cm, and 45mm x 45mm x 15cm. The 45mm x 45mm x 10cm was not implanted during an initial procedure, but was implanted during a reintervention.
[2]All percentages based on number of subjects enrolled.
[3]All percentages based on number of devices implanted.

Table 17. Summary of Number of CTAG Devices per Subject at Initial Procedure

	Malperfusion Subgroup	**Rupture Subgroup**	**TAG 08-01 Cohort**
Number of Enrolled Subjects	39	11	50
Number of Subjects With Successful Initial Implant	39	11	50
Number of Implanted Endoprostheses (Initial Implant)			
1	25 (64.1%)	6 (54.5%)	31 (62.0%)
2	12 (30.8%)	3 (27.3%)	15 (30.0%)
3	2 (5.1%)	1 (9.1%)	3 (6.0%)
4	0 (0.0%)	1 (9.1%)	1 (2.0%)
n	39	11	50
Mean (Std Dev)	1.4 (0.6)	1.7 (1.0)	1.5 (0.7)
Median	1.0	1.0	1.0
Range	(1.0, 3.0)	(1.0, 4.0)	(1.0, 4.0)

Table 18. Summary of Procedural Outcomes

	TAG 08-01 Cohort	**95% CI**
Number of Enrolled Subjects	50	
Procedure Time (minutes)		
n	50	
Mean (Std Dev)	175.3 (99.9)	(147.6, 203.0)
Median	168.0	
Range	(43.0, 467.0)	
Blood Loss (mL)		
n	50	

	TAG 08-01 Cohort	95% CI
Mean (Std Dev)	246.6 (227.9)	(183.4, 309.8)
Median	200.0	
Range	(10.0, 1000)	
Procedure Survival	50 (100.0%)	(92.9%, 100.0%)
Intubation		
Yes	47 (94.0%)	
No	3 (6.0%)	
Additional Procedures at Treatment[1]	26 (52.0%)	
Surgical Fenestration	0 (0.0%)	
Endovascular Fenestration	2 (7.7%)	
Aortic Stenting	2 (7.7%)	
Peripheral Stenting	20 (76.9%)	
Surgical Bypass	4 (15.4%)	
Angioplasty	5 (19.2%)	
Other Procedure	6 (23.1%)	

Confidence Intervals are score intervals for categorical variables, and Wald intervals for continuous variables.
[1]This count used as denominator for percentages under this heading.

Peripheral stenting was defined as a stent or stent graft placed in a vessel branching from the aorta. This can include vessels that come off in the thoracic arch, the mesentery, either of the renal arteries as well as the iliac arteries. The locations of the peripheral stent placements are described in **Table 19**.

Twenty (20) subjects were noted as receiving peripheral stenting. One additional subject (0801-141-008) received a stent in the left carotid artery, but this procedure was categorized by the site into the "Other Procedure" category. For clarity, this subject has been added to the peripheral stenting categorization below. A total of 31 stents (among 28 locations, three classified as "bilateral") were used in 21 subjects. The specific location, as identified by the site, is reported in **Table 19**.

Table 19. Peripheral Stenting Locations

Location of Stenting	Number of Locations	Number of Subjects
Arch Vessel	4	4
Left Carotid	3	-
Right Innominate	1	-
Mesenteric	2	2
Celiac	1	-
Superior Mesenteric	1	-
Renal	8	8
Left Renal	2	-
Right Renal	5	-
Renal	1	-
Iliac	14	11
Bilateral Iliac	2	-
Bilateral Common	1	-
Left Common	2	-
Left External	1	-
Left Iliac	1	-
Right Common	3	-
Right External	3	-
Right Iliac	1	-
Total	28	21

Surgical bypasses with their locations are described in **Table 20**. The four subjects with surgical bypasses consist of one femoral-femoral artery bypass and three left carotid-left subclavian artery bypasses.

Table 20. Surgical Bypass Locations

Type of Bypass	Number of Procedures	Number of Subjects
Left Carotid-Left Subclavian Bypass*	3	3
Femoral-Femoral Artery Bypass	1	1
Total	4	4

* Also reflected in Treatment Characteristics

The locations of the angioplasties observed in this study are described in **Table 21**. Five subjects were noted as receiving angioplasty. One additional subject (0801-134-005) received patch balloon angioplasty to the right common femoral artery, but this procedure was categorized by the site into the "Other Procedure" category. For clarity, this subject has been added to the categorization of angioplasty below. Six subjects experienced balloon angioplasty in nine locations with five reported in the iliac artery bed, two in the mesenteric bed, and two in the femoral bed. The specific location, as identified by the site, is reported.

All but one subject receiving angioplasty received at least one peripheral stent as discussed previously. The location of balloon angioplasty may be in addition to the location of the peripheral stent or stent graft with some subjects treated in multiple areas of the body.

Table 21. Angioplasty Locations

Location of Angioplasty	Number of Procedures	Number of Subjects
Mesenteric	**2**	**2**
Celiac	1	
Superior Mesenteric	1	
Iliac	**5**	**4**
Bilateral Common Iliac	1	
Left External Iliac	1	
Left Internal Iliac	1	
Right Common Iliac	1	
Right Iliac	1	
Femoral	**2**	**2**
Left Common Femoral	1	
Right Common Femoral	1	
Total	9	6

Revascularization of the left subclavian artery is characterized in **Table 22** with 75% of subjects receiving no revascularization following coverage.

Table 22. Summary of Left Subclavian Artery Procedures and Coverage

	LSA COVERAGE		
LSA Procedure	**None**	**Partial**	**Complete**
None	14(28.0%)	8(16.0%)	19(38.0%)
Transposed	0(0.0%)	0(0.0%)	2(4.0%)
Bypassed	0(0.0%)	1(2.0%)	6(12.0%)

A summary of convalescence is presented in **Table 23.** Median hospital stay after endovascular treatment with the CTAG Device was 10 days (range 0-41 days). All subjects had an intensive care unit (ICU) stay. The median length of ICU stay was 4.8 days. Hospital survival rate was 92.0%.

Table 23. Summary of Subject Convalescence

	TAG 08-01 Cohort	95% CI
Number of Enrolled Subjects	50	
Hospitalization Duration (Days)		
n	50	
Mean (Std Dev)	13.8 (9.8)	(11.1, 16.5)
Median	10	
Range	(0, 41.0)	
ICU Stay		
Yes	50 (100.0%)	(92.9%, 100.0%)
No	0 (0.0%)	
ICU Days		
n	50	
Mean (Std Dev)	7.6 (7.4)	(5.6, 9.7)
Median	4.8	
Range	(0.0, 31.8)	
Intubation		
Yes	47 (94.0%)	
No	3 (6.0%)	

	TAG 08-01 Cohort	95% CI
Ventilator Days		
n	50	
Mean (Std Dev)	3.7 (5.9)	
Median	1.0	
Range	(0, 26.0)	
Hospital Survival	46 (92.0%)	

D. Safety and Effectiveness Results

1. Safety Results

Gore evaluated the safety of the CTAG Device through collection of site reported adverse events.

Primary Endpoint Analysis

The primary endpoint for this study was all cause mortality incidence through 30 days post-treatment. The primary endpoint analysis population consisted of all enrolled subjects. Through 30 days post-treatment, a total of four subjects died. Based on this information, there was a probability of 99.8% that the study result met the 30 day mortality performance goal of 25% (**Table 24)**. One additional subject was unable to be located or contacted after leaving the hospital against medical advice and was considered a primary endpoint event. Based on five subjects having primary endpoint events, there was a probability of 99.4% that the study result met the 30 day mortality performance goal of 25% (**Table 25)**. Because this met the 99% probability threshold, enrollment was concluded with enrollment of 50 subjects due to study success.

Table 24. Endpoint Analysis of Known Subjects

Enrolled	Eligible for Primary Endpoint Analysis	Number of 30 Day Deaths	30 Day Mortality Proportion	Protocol Performance Goal	Pr(Mortality<Performance Goal | Data)	Posterior Predictive Probability of Study Success Pr(Success|Data)
50	50	4	0.0800	0.25	0.998	0.987

Table 25. Endpoint Analysis with Non-Responders

Enrolled	Eligible for Primary Endpoint Analysis	Number of 30 Day Deaths	30 Day Mortality Proportion	Protocol Performance Goal	Pr(Mortality<Performance Goal | Data)	Posterior Predictive Probability of Study Success Pr(Success|Data)
50	50	5	0.1000	0.25	0.994	0.962

Subject Deaths

Six TAG 08-01 study subjects have died throughout the course of the study. A listing of individual deaths, with their CEC adjudications, is found in **Table 26.**

Table 26. Death Listing

Subject ID	Study Day	Cause of Death	Relationship of Death to Device or Procedure[1]
0801-120-007	182	Acute myocardial infarction	Unrelated to device or endovascular procedure
0801-126-003	89	Aortic dissection rupture	Indeterminate
0801-135-001	0	Aortic dissection	Related to the endovascular procedure
0801-139-001	0	Aortic rupture	Related to the device and the endovascular procedure
0801-141-008	5	Cerebral ischaemia	Unrelated to device or endovascular procedure
0801-181-008	3	Pulmonary embolism	Related to the endovascular procedure

[1] As adjudicated by CEC

Subject 0801-126-003 presented to the hospital with complaint of a headache. The subject collapsed and was unable to be revived. The autopsy notes a dissecting rupture of the proximal thoracic arch

Subject 0801-135-001 had a retrograde dissection caused by advancement of device delivery catheter with cardiac arrest resulting shortly thereafter.

Subject 0801-139-001 had an aortic rupture shortly after the procedure due to an inability to obtain seal at the primary entry tear.

Subject 0801-181-008 collapsed during a bowel movement. Pulmonary embolism was confirmed as the cause of death via autopsy.

Although there were some deaths related to the device or the procedure, the overall mortality is low.

Serious Adverse Events

Site reported serious adverse events (SAEs) reported by the sites in the first 30 days post-procedure are summarized in **Table 27**. Of the subjects that reported an SAE within 30 days post-procedure, 28 (56%) subjects had at least 1 SAE reported and 18 of those subjects had more than 1 SAE reported. **Table 28** provides information on selected 30 Day SAE results from the TAG 08-01 and the SVS MF.

The most common serious adverse event seen in the study was respiratory failure with 14% of subjects experiencing this within 30 days of the procedure. All other adverse events were observed in less than 10% of subjects. The remaining top three frequent adverse events were cerebrovascular accident (characterized by embolic material), pyrexia (post-implant syndrome) and acute renal failure (most likely secondary to presenting aortic dissection). Device specific events such as stent graft endoleak or complication of device catheter removal were each under 5%.

Table 27. Summary of Serious Adverse Events through 30 Days

	TAG 08-01 Cohort
Number of Enrolled Subjects	50
Any Serious Event	28(56.0%)
Respiratory failure[1]	7(14.0%)
Cerebrovascular accident[2,3]	4(8.0%)
Pyrexia[4]	4(8.0%)
Renal failure acute[5]	4(8.0%)
Hypertension	3(6.0%)
Hypoxia[6]	3(6.0%)
Abdominal pain	2(4.0%)
Acute myocardial infarction[7]	2(4.0%)
Acute respiratory distress syndrome[8]	2(4.0%)
Acute respiratory failure	2(4.0%)
Aortic dissection[9]	2(4.0%)
Atrial fibrillation	2(4.0%)
Back pain	2(4.0%)
Gastrointestinal necrosis	2(4.0%)
Hypotension	2(4.0%)
Pleural effusion	2(4.0%)
Sepsis	2(4.0%)
Stent-graft endoleak[10]	2(4.0%)
Urinary tract infection	2(4.0%)
White blood cell count increased	2(4.0%)
Anaemia	1(2.0%)
Angina pectoris	1(2.0%)
Anuria	1(2.0%)
Aortic rupture[11]	1(2.0%)
Basal ganglia infarction[3]	1(2.0%)
Brain oedema[12]	1(2.0%)
Cardiac failure congestive[12]	1(2.0%)
Carotid artery occlusion[12,13]	1(2.0%)
Cerebral ischaemia[3,12]	1(2.0%)
Compartment syndrome	1(2.0%)
Complication of device removal[14]	1(2.0%)
Constipation	1(2.0%)
Delirium	1(2.0%)
Delirium tremens	1(2.0%)
Encephalopathy	1(2.0%)
Functional gastrointestinal disorder	1(2.0%)
Groin infection[12]	1(2.0%)
Haemothorax	1(2.0%)
Hypocalcaemia	1(2.0%)
Ileus	1(2.0%)
Incision site oedema[12]	1(2.0%)
Incision site pain[12]	1(2.0%)
Ischaemic hepatitis	1(2.0%)
Ischaemic stroke[3,12]	1(2.0%)
Labile blood pressure	1(2.0%)
Lactic acidosis	1(2.0%)
Leukocytosis	1(2.0%)
Mental status changes	1(2.0%)
Metabolic acidosis	1(2.0%)

	TAG 08-01 Cohort
Monoplegia[12]	1(2.0%)
Multi-organ failure	1(2.0%)
Muscular weakness[12]	1(2.0%)
Paraesthesia	1(2.0%)
Paraparesis[12,15]	1(2.0%)
Peptic ulcer	1(2.0%)
Peripheral artery stenosis	1(2.0%)
Pneumonia	1(2.0%)
Pulmonary bulla	1(2.0%)
Pulmonary embolism[12]	1(2.0%)
Pulmonary hypertension	1(2.0%)
Pulmonary oedema[12]	1(2.0%)
Renal failure	1(2.0%)
Renal failure chronic	1(2.0%)
Spinal cord ischaemia[15]	1(2.0%)
Troponin increased	1(2.0%)
Unresponsive to stimuli	1(2.0%)
Vomiting	1(2.0%)

[1]Two of these events were adjudicated by the CEC to be related to the endovascular procedure
[2]All four of these events were adjudicated by the CEC to be related to the endovascular procedure
[3]Identified as stroke; additional information on all stroke events is provided below in the *Additional Adverse Event Information* section.
[4]Two of these events were adjudicated by the CEC to be related to the endovascular procedure
[5]Two of these events were adjudicated by the CEC to be related to the endovascular procedure; it is unknown if the events were related to contrast dye
[6]One of these events was adjudicated by the CEC to be related to the endovascular procedure
[7]One of these events was adjudicated by the CEC to be related to the endovascular procedure
[8]One of these events was adjudicated by the CEC to be related to the endovascular procedure
[9]Additional information on all progressive aortic dissection events is provided below in the *Additional Adverse Event Information* section; one event was CEC adjudicated as related to the endovascular procedure; one event was CEC adjudicated as related to both the device and endovascular procedure
[10] Additional information on stent graft endoleaks available in **Table 44** Major Device Events by Follow-Up Period; one Type IA endoleak was CEC adjudicated as related to both the device and endovascular procedure; the other event was reported by the site as persistent blood flow in the false lumen was determined by the CEC to be unrelated to device or endovascular procedure
[11]Additional information on rupture events available in **Table 43** Aortic Rupture Events
[12]This event was adjudicated by the CEC to be related to the endovascular procedure
[13]Following device deployment, a hemodynamic compromise was observed; a stent was deployed in the left common carotid artery to ensure vessel patency
[14]Additional information on the complication of device removal is available in **Table 44**; this event was adjudicated by the CEC to be related to both the device and endovascular procedure
[15]Additional information on paraparesis and spinal cord ischaemia events is provided below in the *Additional Adverse Event Information* section;

Table 28. Selected 30 Day SAE Results from TAG 08-01 and the SVS MF

	TAG 08-01 Cohort	SVS MF Cohort
Number of Enrolled Subjects	50	85
Any Event	20(40.0%)	32(37.6%)
Death	4(8.0%)	9(10.6%)
MI	2(4.0%)	1(1.2%)
Stroke1	7(14.0%)	8(9.4%)
Renal Failure (+Dialysis)	3(6.0%)	8(9.4%)
Respiratory Failure (with Ventilation)	9(18.0%)	2(2.4%)
Paralysis/Paraparesis	3(6.0%)	8(9.4%)
Bowel Ischemia	2(4.0%)	3(3.5%)

[1] Two non-serious strokes were excluded from TAG 08-01 cohort as the SVS Publication only included serious strokes.

Sites were instructed to report and classify severity of all adverse events as shown in **Table 29**.

Table 29. Serious Adverse Events by Follow-Up Period

	Post-Treatment Follow-up Period					
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**
Blood and lymphatic system disorders	0(0.0%)	1(2.1%)	1(2.2%)	1(2.2%)	0(0.0%)	2(9.1%)
Anaemia	-	1(2.1%)	-	-	-	2(9.1%)
Disseminated intravascular coagulation	-	-	-	1(2.2%)	-	-
Leukocytosis	-	-	1(2.2%)	-	-	-
Metabolism and nutrition disorders	2(4.0%)	1(2.1%)	0(0.0%)	1(2.2%)	0(0.0%)	0(0.0%)
Lactic acidosis	1(2.0%)	-	-	-	-	-
Metabolic acidosis	1(2.0%)	-	-	-	-	-
Hypocalcaemia	-	1(2.1%)	-	-	-	-
Gout	-	-	-	1(2.2%)	-	-

	Post-Treatment Follow-up Period					
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**
Psychiatric disorders	0(0.0%)	3(6.3%)	0(0.0%)	1(2.2%)	0(0.0%)	0(0.0%)
Delirium	-	1(2.1%)	-	-	-	-
Delirium tremens	-	1(2.1%)	-	-	-	-
Depression	-	-	-	1(2.2%)	-	-
Mental status changes	-	1(2.1%)	-	-	-	-
Nervous system disorders	4(8.0%)	8(16.7%)	1(2.2%)	1(2.2%)	2(4.8%)	1(4.5%)
Cerebrovascular accident	0(0.0%)	4(8.3%)	-	-	-	-
Basal ganglia infarction	0(0.0%)	1(2.1%)	-	-	-	-
Carotid artery occlusion	1(2.0%)	0(0.0%)	-	-	-	-
Cerebral ischaemia	0(0.0%)	1(2.1%)	-	-	-	-
Ischaemic stroke	0(0.0%)	1(2.1%)	-	-	-	-
Spinal cord ischaemia	1(2.0%)	-	-	1(2.2%)	-	0(0.0%)
Spinal cord infarction	0(0.0%)	-	-	0(0.0%)	-	1(4.5%)
Monoplegia	0(0.0%)	1(2.1%)	-	-	-	-
Paraparesis	1(2.0%)	0(0.0%)	-	-	-	-
Encephalopathy	-	1(2.1%)	-	-	-	-
Brain oedema	-	1(2.1%)	-	-	-	-
Unresponsive to stimuli	-	-	1(2.2%)	-	-	-
Paraesthesia	1(2.0%)	-	-	-	-	-
Convulsion	-	-	-	-	1(2.4%)	-
Brain injury	-	-	-	-	1(2.4%)	-
Cardiac disorders	0(0.0%)	4(8.3%)	0(0.0%)	5(11.1%)	4(9.5%)	2(9.1%)
Angina pectoris	-	1(2.1%)	-	3(6.7%)	3(7.1%)	1(4.5%)
Acute myocardial infarction	-	2(4.2%)	-	1(2.2%)	0(0.0%)	0(0.0%)
Cardiac failure congestive	-	1(2.1%)	-	-	-	1(4.5%)
Atrial fibrillation	-	2(4.2%)	-	-	-	-

	Post-Treatment Follow-up Period					
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**
Cardiac arrest	-	-	-	1(2.2%)	1(2.4%)	-
Vascular disorders	3(6.0%)	6(12.5%)	1(2.2%)	3(6.7%)	0(0.0%)	3(13.6%)
Aortic aneurysm	0(0.0%)	0(0.0%)	1(2.2%)	0(0.0%)	-	1(4.5%)
Aortic dissection	1(2.0%)	1(2.1%)	0(0.0%)	0(0.0%)	-	0(0.0%)
Aortic dissection rupture	0(0.0%)	0(0.0%)	0(0.0%)	1(2.2%)	-	0(0.0%)
False lumen dilatation of aortic dissection	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	-	1(4.5%)
Hypertension	-	3(6.3%)	-	-	-	-
Hypotension	-	2(4.2%)	-	-	-	-
Accelerated hypertension	-	-	-	-	-	1(4.5%)
Labile blood pressure	-	1(2.1%)	-	-	-	-
Haemorrhage	-	-	-	1(2.2%)	-	-
Deep vein thrombosis	-	-	-	1(2.2%)	-	-
Peripheral artery stenosis	1(2.0%)	-	-	-	-	-
Aortic rupture	1(2.0%)	-	-	-	-	-
Respiratory, thoracic and mediastinal disorders	3(6.0%)	13(27.1%)	1(2.2%)	1(2.2%)	1(2.4%)	2(9.1%)
Respiratory failure	-	7(14.6%)	-	1(2.2%)	-	-
Acute respiratory failure	-	2(4.2%)	-	0(0.0%)	-	-
Pleural effusion	1(2.0%)	1(2.1%)	-	-	-	1(4.5%)
Haemothorax	0(0.0%)	1(2.1%)	-	-	-	0(0.0%)
Pneumothorax	0(0.0%)	0(0.0%)	-	-	-	1(4.5%)
Hypoxia	-	2(4.2%)	1(2.2%)	-	1(2.4%)	-
Acute respiratory distress syndrome	1(2.0%)	1(2.1%)	-	-	-	-
Pulmonary oedema	0(0.0%)	1(2.1%)	-	-	-	-
Pneumonitis	-	-	-	-	1(2.4%)	-
Pulmonary bulla	1(2.0%)	-	-	-	-	-

	Post-Treatment Follow-up Period					
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**
Pulmonary hypertension	-	1(2.1%)	-	-	-	-
Pulmonary embolism	-	1(2.1%)	-	-	-	-
Gastrointestinal disorders	2(4.0%)	4(8.3%)	2(4.4%)	2(4.4%)	1(2.4%)	2(9.1%)
Abdominal pain	-	1(2.1%)	1(2.2%)	1(2.2%)	-	-
Haematemesis	-	-	0(0.0%)	1(2.2%)	-	0(0.0%)
Lower gastrointestinal haemorrhage	-	-	0(0.0%)	0(0.0%)	-	1(4.5%)
Upper gastrointestinal haemorrhage	-	-	1(2.2%)	0(0.0%)	-	0(0.0%)
Gastrointestinal necrosis	-	2(4.2%)	-	-	-	-
Ileus	1(2.0%)	-	-	-	-	1(4.5%)
Vomiting	-	-	1(2.2%)	-	1(2.4%)	1(4.5%)
Nausea	-	-	0(0.0%)	-	1(2.4%)	0(0.0%)
Pancreatitis	-	-	1(2.2%)	-	-	-
Small intestinal obstruction	-	-	-	1(2.2%)	-	-
Abdominal distension	-	-	-	-	-	1(4.5%)
Constipation	-	-	1(2.2%)	-	-	-
Functional gastrointestinal disorder	1(2.0%)	-	-	-	-	-
Peptic ulcer	-	1(2.1%)	-	-	-	-
Hepatobiliary disorders	1(2.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Ischaemic hepatitis	1(2.0%)	-	-	-	-	-
Musculoskeletal and connective tissue disorders	2(4.0%)	0(0.0%)	2(4.4%)	1(2.2%)	0(0.0%)	2(9.1%)
Back pain	-	-	2(4.4%)	-	-	1(4.5%)
Haemarthrosis	-	-	-	1(2.2%)	-	-
Muscular weakness	1(2.0%)	-	-	-	-	-
Compartment syndrome	1(2.0%)	-	-	-	-	-

	Post-Treatment Follow-up Period					
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**
Osteoarthritis	-	-	-	-	-	1(4.5%)
Renal and urinary disorders	2(4.0%)	3(6.3%)	2(4.4%)	0(0.0%)	0(0.0%)	1(4.5%)
Renal failure acute	1(2.0%)	3(6.3%)	1(2.2%)	-	-	0(0.0%)
Anuria	1(2.0%)	0(0.0%)	0(0.0%)	-	-	0(0.0%)
Renal failure	1(2.0%)	0(0.0%)	0(0.0%)	-	-	0(0.0%)
Renal failure chronic	0(0.0%)	0(0.0%)	1(2.2%)	-	-	0(0.0%)
Renal impairment	0(0.0%)	0(0.0%)	0(0.0%)	-	-	1(4.5%)
General disorders and administration site conditions	2(4.0%)	6(12.5%)	1(2.2%)	1(2.2%)	0(0.0%)	0(0.0%)
Pyrexia	-	4(8.3%)	-	-	-	-
Stent-graft endoleak	1(2.0%)	1(2.1%)	1(2.2%)	1(2.2%)	-	-
Complication of device removal	1(2.0%)	-	-	-	-	-
Multi-organ failure	-	1(2.1%)	-	-	-	-
Investigations	0(0.0%)	2(4.2%)	1(2.2%)	0(0.0%)	0(0.0%)	0(0.0%)
White blood cell count increased	-	1(2.1%)	1(2.2%)	-	-	-
Troponin increased	-	1(2.1%)	-	-	-	-
Injury, poisoning and procedural complications	0(0.0%)	2(4.2%)	0(0.0%)	2(4.4%)	0(0.0%)	0(0.0%)
Incision site oedema	-	1(2.1%)	-	-	-	-
Incision site pain	-	1(2.1%)	-	-	-	-
Vascular pseudoaneurysm	-	-	-	1(2.2%)	-	-
Lumbar vertebral fracture	-	-	-	1(2.2%)	-	-

Note: Column header counts and denominators are the number of subjects at risk at the start of each interval. Entries represent MedRA SOC, HLT and PT and are identified by increasing level of indentation.
Study period definitions: Procedure(0-0 days) Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days)
MedDRA Version: V15.1

Additional Adverse Event Information

In order to provide further clarity on adverse events of particular interest in the setting of endovascular treatment of acute complicated Type B aortic dissection, further detailed information has been compiled on stroke, spinal cord ischemia, and aortic dissection events subsequent to the initial endovascular procedure.

Stroke

Stroke (regardless of severity status) was reported in 9 subjects in the TAG 08-01 study (18%): all occurring within the first 30 days after treatment. Seven of these were classified as serious events and were reported in **Tables 27** and **29** as cerebrovascular accident, basal ganglia infarction, cerebral ischemia, or ischemic stroke. Events classified as stroke could have been identified by clinical symptoms that may or may not have included a follow-up evaluation by a neurologist, radiographic imaging or a combination of both types of assessments. Adverse event descriptions, as reported by the investigational sites, with Investigator evaluated event severities and the corresponding CEC adjudications are provided in **Table 30**.

Table 30. Stroke Data

Subject Number	Event Day	Adverse Event Description	Serious Non-serious	CEC Adjudication
0801-103-002	10	Age indeterminate infarct of right cerebellum and basal ganglia	Serious	Unrelated to device or endovascular procedure
0801-112-005	6	Multiple brain infarcts	Non-serious	Related to the endovascular procedure
0801-120-003	2	Cerebrovascular accident	Serious	Related to the endovascular procedure
0801-134-005	5	Intraventricular hemorrhage	Non-serious	Unrelated to device or endovascular procedure
0801-141-008	5	Diffuse cerebral anoxic ischemic injury	Serious	Related to the endovascular procedure
0801-146-002	1	Ischemic changes in left frontal and occipital lobes of brain without hemmorrhage consistent with stroke	Serious	Related to the endovascular procedure
0801-178-001	9	Stroke	Serious	Related to the endovascular procedure
0801-306-003	1	Bilateral strokes	Serious	Related to the endovascular procedure
0801-361-021	1	CVA due to multiple embolic infarctions through out the brain bilaterally without hemorrhage.	Serious	Related to the endovascular procedure

An independent review of the stroke events was conducted by two neurologists as part of the study's CEC. Using site provided source documentation, they assessed events for the type of stroke observed, the presence of confounding factors potentially contributing to the event, the status of event symptoms at time of discharge, the status of event symptoms at time of the last available follow-up visit, and evaluated the overall impact the event had on subject functional outcomes. Functional outcome was defined as event impact in terms of altering the ability for the subject to carry out normal daily activities in the medical

opinion of the CEC neurologists. A summary of their findings can be found in **Table 31.**

Table 31. CEC Neurologist Stroke Review

Subject Number	Stroke Type	Confounding Event Factors	Improvement-Discharge	Improvement-Follow-up	Impact on Functional Outcome
0801-103-002	Ischemic-Embolic	ICU delirium/medications	Yes-Full	N/A- Insufficient information	None
0801-112-005	Ischemic-Embolic	Hypoxia	Yes-Full	Yes-Full	None
0801-120-003	Ischemic-Embolic	Questionable occlusion of left subclavian and vertebral arteries	Yes-Partial	Yes-Partial	Moderate
0801-134-005	Hemorrhagic	Heparin-during procedure	Yes-Full	Yes-Full	None[1]
0801-141-008	Ischemic-hemodynamic/perfusional in origin	None	N/A- Death	N/A- Death	Severe
0801-146-002	Ischemic-Embolic	None	Yes-Partial	Yes-Full	None
0801-178-001	Ischemic-Embolic	Retrograde ascending aortic dissection	Yes-Partial	Yes-Full	None
0801-306-003	Ischemic-Embolic	Diffuse atherosclerotic arch	Yes-Partial	Yes-Full	None
0801-361-021	Ischemic-Embolic	None	Yes-Partial	Yes-Full	None[1]

[1] A functional limitation is present but related to a spinal cord infarction that occurred either before or after the procedure.

Of the nine neurological events that were reviewed by the CEC subcommittee, eight were characterized as ischemic in nature, with one as hemorrhagic. Of the ischemic strokes, all but one were seen in the presence of an embolic component. Five of the eight subjects with ischemic stroke had confounding factors that could have contributed to the strokes as identified by CEC subcommittee review. Improvement in neurological symptoms was seen in eight subjects over the course of the study. In the short term, 88.8% (8/9) experienced an improvement of neurological symptoms prior to discharge. Functional outcome, as an estimate of quality of life, was approximated using available follow-up physical examination information. No functional impact as a direct result of neurological symptoms was seen in seven subjects (7/9, 77.7%) and one subject with moderate impact. The remaining subject, with a severe impact, died during their initial hospitalization following a significant period of ischemia due to the aortic dissection process leading to compromise in multiple body systems. The overall stroke rate observed in the study was 18% (9/50); however only 4% (2/50) were disabling.

Spinal Cord Ischemia

A total of four spinal cord ischemia events were observed in the TAG 08-01 subjects. The events are summarized below.

- A subject developed spinal cord ischemia which was identified on day 1 post-op. A lumbar drain was placed in addition to medications administered. The event resolved the next day.
- A subject presented with an ischemia of the spinal cord that was exacerbated with the procedure. Following the operation, a spinal drain was placed and the mean arterial pressure was elevated. The event has not resolved with the subject remaining with a partial neurological deficit. The functional deficits included loss of strength in left side. At discharge on post-operative day (POD) 23, the subject had regained strength in his left side but had persistent left foot drop accompanied with some difficulty walking. He was able to perform all activities of daily living with his left side. The subject's foot drop had notably improved by his follow-up visit on POD 259 and he no longer required a brace or any assistive devices for walking.
- A subject developed spinal cord ischemia which was identified on day 1 post-op. A lumbar drain was placed and the event resolved on day 3 post-op.
- A subject developed spinal cord ischemia on day 85 post-op following an abdominal debranching procedure to treat persistent flow in the false lumen. The event resolved four days later.

Of importance, 3 out of 4 cases resolved with prompt insertion of cerebro-spinal fluid (CSF) drain and only one subject developed a permanent deficit.

Paraplegia/Paraparesis/Monoplegia

A total of four paraplegia/paraparesis/monoplegia events were observed in the TAG 08-01 subjects. The events are summarized below.

- A subject experienced a spinal cord infarct, resulting in complete lower extremity paralysis, on POD 678 following open thoracoabdominal surgery to treat an expanding aortic false lumen.
- A subject experienced bilateral lower extremity paraparesis immediately following the procedure. On POD 1, the subject was taken back to the operating room for the placement of multiple stents in the right iliac artery. The paraparesis resolved on POD 62.
- A subject presented with neurological compromise of the lower extremities that was exacerbated following the procedure. Medications were adjusted and a consultation done with neurology. The adverse event resolved on POD 4.
- On POD 4, a subject experienced monoplegia (unable to move left leg). A CSF drain was placed as treatment for the monoplegia and the event resolved.

Progressive Aortic Dissection

Progressive aortic dissection (including retrograde type A dissection) was reported in a total of five subjects in the TAG 08-01 study. Four of these were classified as serious events, two of which occurred within 30 days of procedure and were reported in **Table 27** as aortic dissections. Event descriptions as reported by the investigational sites for these events are provided in **Table 32**.

Table 32. Progressive Aortic Dissection Data

Subject Number	Event Day	Event Description	Potential Mechanism as Determined by Sponsor	CEC Causality Adjudication	Outcome
0801-126-003	89	Rupture dissecting Type A2 aneurysm of the proximal aortic arch	Disease Progression	Indeterminate	Death
0801-130-001	183	Subject 001 developed pseudoaneurysm of ascending aorta related to tear 1 cm above sinotubular junction (diameter 8-9 cm). Subject required emergent ascending/arch reconstruction sewn to CTAG distally.	Disease Progression	Unrelated to device or endovascular procedure	Ascending aortic replacement, subject recovered.
0801-135-001	0	Retrograde dissection	Iatrogenic	Related to endovascular procedure	Death
0801-140-004	29	Retrograde Type A aortic dissection	Unknown	Indeterminate	No further treatment
0801-178-001	6	Retrograde ascending aortic dissection	Procedural or Device	Related to device and endovascular procedure	Ascending aortic replacement, subject recovered.

Of the five Type A dissection events, two are most likely due to disease progression, one event due to an iatrogenic cause, one event that could be related to either a device or procedural cause and one event lacking enough information to make an inference. These events support the need for cautious manipulation of friable dissected aorta and the necessity of strict blood pressure management following the procedure to limit progression of the dissection.

Safety Subgroup Analysis (Gender)

A post hoc analysis of SAEs and death by gender was performed. These results are presented in **Tables 33** and **34.** While the study was not originally designed or powered for this analysis, no significant differences in overall mortality or 30 day SAEs were noted between males and females.

Table 33. Frequency of 30 Day Serious Adverse Events by Gender

	All	Females	Males	P-value*
Number of Enrolled Subjects	50	13	37	
Any 30-Day Serious Adverse Event				0.339
Yes	28(56.0%)	9(69.2%)	19(51.4%)	
No	22(44.0%)	4(30.8%)	18(48.6%)	

* P-value derived from Fisher's Exact test

Table 34. Frequency of Mortality by Gender

	All	Females	Males	P-value*
Number of Enrolled Subjects	50	13	37	
Any Mortality				0.643
Yes	6(12.0%)	2(15.4%)	4(10.8%)	
No	44(88.0%)	11(84.6%)	33(89.2%)	

* P-value derived from Fisher's Exact test

Safety Discussion

The TAG 08-01 study was designed primarily to establish that mortality at 30 days following treatment with the CTAG Device was lower than the protocol defined performance goal of 25%. The study data have established that there is a low probability (<0.01) that 30 day mortality following implantation of the CTAG Device is >25%.

The safety events observed during the TAG 08-01 study and follow-up are anticipated complications of stent graft placement in aortic dissection patients. Of note, the stroke rate was higher than expected but these events did not result in a severe, activity-limiting state as most patients exhibited full recovery with no greater impact than exhibited by their acute dissection. In general, subjects survived the procedure and required little additional intervention in the peri-operative period to address their presenting maladies.

2. Effectiveness Evaluation

The TAG 08-01 protocol specified primary and secondary effectiveness endpoints that were evaluated using descriptive statistics. The primary effectiveness endpoint was closure of the primary entry tear at the 1 month follow-up visit. Secondary effectiveness endpoints included false lumen thrombosis (assessed by the Core Lab), additional dissection-based intervention and aortic rupture through the course of available follow-up.

In addition to these effectiveness endpoints, information on device events were collected as reported by the sites based on interpretation of follow-up imaging and the definitions of events included in the TAG 08-01 protocol.

A severity categorization (major or minor) was assigned to all adverse device events. This determination was made by the site and select events, including all major adverse events (MAEs) and major device events (MDEs), were adjudicated by the CEC. For the purpose of this effectiveness analysis, the adjudicated severity is displayed for cases in which CEC adjudication was required; otherwise the site-reported severity is displayed.

Adverse events were characterized by severity, e.g., major or minor, as defined below:

Major
- Requires therapy, minor hospitalization (< 48 hours), or
- Major therapy, unplanned increase in level of care, prolonged hospitalization (> 48 hours), or
- Permanent adverse sequelae, or
- Death

Minor
- Requires no therapy, no consequence, or
- Nominal therapy, no consequence; includes overnight admission for observation only

In addition, an independent Core Lab received CT scans and X-rays performed by the sites and conducted an independent review of these images to further characterize device performance and aortic remodeling.

Primary Effectiveness Endpoint Analysis

The analysis of primary entry tear closure was performed using the Effectiveness Eligible population. This was defined as subjects who completed the 1 month follow-up visit with any CT or MR imaging provided to the Core Lab for analysis within the 1 month analysis window (15-59 days). Contrast enhanced CT angiography was used to evaluate for exclusion of the primary entry tear.

Summary historical data for closure of the primary entry tear were provided in the TAG 08-01 protocol and are replicated in **Table 35**. Results from the TAG 08-01 study are provided in **Table 36**. The percentage of TAG 08-01 subjects with successful closure of the primary entry tear at 30 days post-procedure (97.5%) is within the range of historically reported results. The one subject with failure to exclude the primary entry tear was subject 0801-140-004 who had an ongoing untreated retrograde Type A dissection. Effectiveness continued with an observed exclusion rate of 100% at 12 months (**Table 37**).

Table 35. Historical Data for Closure of the Primary Entry Tear

Study	N	% Primary Entry Tear Exclusion
Dake[3]	19	95%
Attia[4]	6	100%
Caronno[5]	5	100%
Dialetto[6]	28	100%
Duebener[7]	10	90%
Iannelli[8]	8	100%
Schoder[9]	28	86%
Steingruber[10]	35	83%
Palma[11]	70	93%
Hutschala[12]	9	100%
Lee[13]	46	85%
Bortone[14]	43	93%
Tiesenhausen[15]	7	100%
Won[16]	12	83%
Kim[17]	72	88%
Chang[18]	1246	89%
Pearce[19]	15	93%
Verhoye[20]	16	100%

Table 36. Primary Effectiveness Endpoint Results: Primary Entry Tear Closure at 30 Days

Enrolled	Eligible for Primary Endpoint Analysis	Primary Entry Tear Exclusion	Percent Primary Entry Tear Exclusion (95% CI)
50	40	39	97.5% (87.1%, 99.6%)

Ten subjects were unavailable for analysis at 30 days due to death (4 confirmed deaths and 1 with unknown vital status), imaging conducted outside of visit window (3), or scan quality (lack of contrast dye or poor visualization) (2). Four out of these five latter subjects were evaluated at 6 months with exclusion of the primary entry tear verified.

Table 37. Primary Entry Tear Closure at 12 Months

Enrolled	Eligible for Analysis	Primary Entry Tear Exclusion	Percent Primary Entry Tear Exclusion (95% CI)
50	37	37	100.0% (90.6%, 100.0%)

Secondary Effectiveness Endpoint Analyses

False Lumen Thrombosis

Summary historical data for closure of the primary entry tear were provided in the TAG 08-01 protocol and are replicated in **Table 38**.

False lumen thrombosis was assessed by the Core Lab. All subjects with imaging follow-up were included in the analyses of false lumen thrombosis and reported in **Table 39**.

Table 38. Historical Data for False Lumen Thrombosis

Study	N	% Complete Thrombosis	% Partial Thrombosis
Dake[3]	19	79%	21%
Attia[4]	5	60%	
Caronno[5]	5	100%	
Dialetto[6]	28	75%	
Schoder[9]	20	90%	
Hutschala[12]	9	22%	78%
Lee[13] (Acute)	19	74%	
Won[16]	12	83%	
Kim[17]	47	75%	
Chang[18]	431	84%	
Pearce[19] (Post Tx)	10	80%	
Pearce[19] (6 Month)	7	100%	
Verhoye[20]	16	25%	38%
Manning[21]	28	82%	
Gaxotte[22] (Discharge)	47	42%	
Gaxotte[22] (F/Up)	41	61%	39%
Hansen[23]	16	100%	

Table 39. Core Lab Reported Data for False Lumen Thrombosis

	Post Treatment Follow up Period								
	Post-Procedure	1 Month	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	Last Follow Up
Number of Subjects	48	45	45	42	22	1	0	0	45
Subjects with CT/MR Assessment	33	41	39	37	18	0	0	0	45
False Lumen Thrombosis Adjacent to Stent Graft									
No Thrombosis	2(6.1%)	0(0.0%)	2(5.1%)	1(2.7%)	0(0.0%)	-	-	-	0(0.0%)
Partial Thrombosis	13(39.4%)	13(31.7%)	9(23.1%)	6(16.2%)	5(27.8%)	-	-	-	9(20.0%)
Complete Thrombosis	14(42.4%)	26(63.4%)	24(61.5%)	28(75.7%)	13(72.2%)	-	-	-	33(73.3%)
Unknown	4(12.1%)	2(4.9%)	4(10.3%)	2(5.4%)	0(0.0%)	-	-	-	3(6.7%)

Median follow-up (procedure to last known contact date) was 497 days. The percentage of complete thrombosis at a level adjacent to the stent graft at the last available follow-up visit (73.3%) is comparable to the results published in the medical literature.

Additional Dissection-Based Intervention

Additional dissection-based intervention was analyzed for all enrolled subjects. Major adverse events that occurred within one year of procedure were adjudicated by the CEC to determine dissection relatedness (i.e., related to malperfusion, rupture or both) or unrelated. Events that occurred one year after the procedure were characterized by a sponsor review. For adverse events deemed by the CEC to be dissection related, all treatments associated with these AEs were considered additional dissection-based interventions (with the exception of events coded as "Other treatment or procedure"). Summary historical data on additional dissection-based interventions were provided in the TAG 08-01 protocol and are replicated in **Table 40**. Site reported data is summarized in **Table 41**. All

additional thoracic stent graft placements are captured under the heading of "TAG Device"; these include both the TAG and CTAG Devices.

Table 40. Historical Data for Additional Dissection-Based Intervention

Study	N	% Dissection Based Intervention
Attia[4]	6*	17%
Duebener[7]	10	50%
Neuhauser[24]	28*	14%
Schoder[9]	24	25%
Steingruber[10]	35*	11%
Kim[17]	70*	13%
Verhoye[20]	16	19%
Manning[21]	28	22%
Pitton[25]	13	46%
Hansen[23]	16	44%

* Data includes only interventions related to additional implants/conversions

Table 41. Additional Dissection-Based Interventions

	Post-Treatment Follow-up Period									
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total Subjects**
Number of Subjects	50	48	45	45	42	22	1	0	0	50
Subjects Receiving Any Additional Dissection Based Intervention	1(2.0%)	5(10.4%)	0(0.0%)	0(0.0%)	0(0.0%)	2(9.1%)	0(0.0%)	-	-	7(14.0%)
95% Confidence Interval										(7.0%,26.2%)
Conversion to open repair	0(0.0%)	0(0.0%)	-	-	-	0(0.0%)	-	-	-	0(0.0%)
Additional TAG device	0(0.0%)	1(2.1%)	-	-	-	0(0.0%)	-	-	-	1(2.0%)
Additional aortic endograft	0(0.0%)	0(0.0%)	-	-	-	0(0.0%)	-	-	-	0(0.0%)
Fenestration	0(0.0%)	1(2.1%)	-	-	-	0(0.0%)	-	-	-	1(2.0%)
Peripheral stenting	0(0.0%)	1(2.1%)	-	-	-	0(0.0%)	-	-	-	1(2.0%)
Surgical bypass	0(0.0%)	0(0.0%)	-	-	-	0(0.0%)	-	-	-	0(0.0%)
Other surgery	1(2.0%)	4(8.3%)	-	-	-	0(0.0%)	-	-	-	4(8.0%)
Other treatment or procedure	0(0.0%)	0(0.0%)	-	-	-	2(9.1%)	-	-	-	2(4.0%)

A total of seven subjects (14%) underwent ten procedures following CTAG Device implant that were directly associated with the original, presenting aortic dissection as determined by the CEC or site Investigators. These ten procedures are described below.

- An additional TAG Device was implanted in one subject. On POD 2, subject 0801-118-002 was taken back to the operating room for an additional CTAG Device to treat persistent flow in the false lumen as a result of a large fenestration distal to the original device. This subject also had an additional surgery as detailed below.
- A fenestration procedure was conducted in one subject. On POD 1, subject 0801-336-001 returned to the operating room for a fenestration of the septum dividing the two aortic channels to treat the observed renal failure. This subject also had an additional surgery as detailed below.

- Peripheral stenting was performed in one subject. On POD 4, subject 0801-120-005 was taken back to the operating room for the placement of a stent to treat a stenosis in the iliac artery.
- Four subjects had additional dissection-based interventions categorized by the sites as other surgeries.
  - On POD 2, subject 0801-103-002 was taken back to the operating room for an open exploratory laparotomy to investigate lactic acidosis and underwent a resection of the right colon due to gastrointestinal necrosis.
  - Subject 0801-141-008 underwent three separate procedures. On the day of the procedure, the subject underwent a fasciotomy of the left lower extremity due to an observed compartment syndrome. On POD 2, the subject had an exploratory laparotomy with total abdominal colectomy. On POD 4, the subject returned again to the operating room for removal and replacement of vacuum dressings, excision of the small bowel and a thorough washout of the abdominal cavity.
  - On POD 13, subject 0801-118-002 had a decortication procedure conducted for a persistent hemothorax. This subject also had an additional TAG Device implant as detailed above.
  - On POD 1, subject 0801-336-001 returned to the operating room for an endarterectomy of both renal arteries to treat anuria. This subject also had a fenestration as detailed above.
- Two subjects had additional dissection-based interventions categorized by the sites as other treatment or procedure.
  - On POD 676, subject 0801-112-005 underwent an open thoracoabdominal repair to treat an enlarging false lumen. The CTAG Device was left in place. The treating surgeon noted false lumen growth of 1.5cm in diameter from a previous evaluation.
  - On POD 861, subject 0801-134-001 received an abdominal stent graft cuff and an iliac stent graft limb to exclude patent fenestrations that were contributing to false lumen growth distal to the previously placed CTAG Device.

Aortic Rupture

A survey of published data on the incidence of aortic rupture following TEVAR for Type B aortic dissection is provided in **Table 42**. The observed frequency of aortic rupture in the TAG 08-01 study (4%) is within the range of these historical results.

Table 42. Historical Data for Aortic Rupture

Study	N	% Rupture
Dake[3]	19	11%
Attia[4]	6	17%
Dialetto[6]	28	4%
Schoder[9]	28	4%
Steingruber[10]	35	3%
Hutschala[12]	9	0
Pearce[19]	7	0
Verhoye[20]	16	13%
Manning[21]	28	7%
Hansen[23]	16	6.3%

Aortic rupture was reported by the investigational sites as an adverse event. Two events of aortic rupture were reported by sites over the duration of the study. A listing of the subjects who experienced aortic rupture can be found in **Table 43**. Events characterized as "aortic rupture" are reported irrespective of their locations in the thoracic aorta (ascending/descending) and their causality.

- Subject 0801-139-001 had an aortic rupture shortly after the procedure due to an inability to obtain seal at the primary entry tear.
- Subject 0801-126-003 presented to the hospital with complaint of a headache. The subject collapsed and was unable to be revived. The autopsy notes a dissecting rupture of the proximal thoracic arch.

Table 43. Aortic Rupture Events

Subject ID	Study Day	System Organ Class / Preferred Term / Adverse Event	Severity	Serious
0801-126-003	89	Vascular disorders / Aortic dissection rupture / Rupture dissecting Type AII aneurysm of the proximal aortic arch	Major	Yes
0801-139-001	0	Vascular disorders / Aortic rupture / Aortic rupture	Major	Yes

Device Events

The study protocol defined a list of anticipated device adverse events which included endoleak, access and deployment failure, lumen obstruction (including device compression and thrombus), prosthesis material failure, extrusion/erosion, prosthesis migration, intercomponent migration and wire fracture. In addition to these events, other potential device events are included which are not specified as part of the enumerated list of events. In the setting of aortic dissection, retrograde aortic dissection and aortic rupture may be considered device events and are therefore included even though they are not events specified in the protocol as device events. The remaining event in this table, complication of delivery catheter removal, was also included in the assessment of device performance since this was reported as an unanticipated adverse device effect.

These events, categorized by severity of major or minor, as well as other events of interest can be found in **Table 44** and **Table 45**.

Table 44. Major Device Events by Follow-Up Period

	Post-Treatment Follow-up Period									
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total**
Number of Subjects	50	48	45	45	42	22	1	0	0	50
Number of Subjects with Imaging Evaluation	50	41	43	40	39	20	0	-	-	50
Any Major Device Event	3(6.0%)	1(2.4%)	0(0.0%)	2(5.0%)	0(0.0%)	0(0.0%)	-	-	-	6(12.0%)
Stent Graft Endoleak[1]	1(2.0%)	0(0.0%)	-	1(2.5%)	-	-	-	-	-	2(4.0%)
Stent-graft endoleak type IA	1(2.0%)	-	-	1(2.5%)	-	-	-	-	-	2(4.0%)
Stent-graft endoleak type II[1]	0(0.0%)	-	-	1(2.5%)	-	-	-	-	-	1(2.0%)
Ascending aortic dissection rupture[2]	0(0.0%)	0(0.0%)	-	1(2.5%)	-	-	-	-	-	1(2.0%)
Complication of device removal[3]	1(2.0%)	0(0.0%)	-	0(0.0%)	-	-	-	-	-	1(2.0%)
Descending thoracic aorta rupture[4]	1(2.0%)	0(0.0%)	-	0(0.0%)	-	-	-	-	-	1(2.0%)
Retrograde aortic dissection[5]	1(2.0%)	1(2.4%)	-	0(0.0%)	-	-	-	-	-	2(4.0%)

Endoleaks are only reported in the time interval in which the event was first observed. The sum of the type of endoleaks may add up to more than the number of subjects with endoleaks, for subjects can have multiple types.
[1]Endoleak originating from the left subclavian artery.
[2]More details on subject 0801-126-003 can be found in the Progressive Aortic Dissection section, **Table 26**, and **Table 43**.
[3]Complication associated with removal of device delivery catheter following successful deployment of the stent graft.
[4]More details on subject 0801-139-001 can be found in **Table 43**.
[5]More details on subjects 0801-135-001 and 0801-178-001 can be found in the Progressive Aortic Dissection section and **Table 26**.

Table 45. Minor Device Events by Follow-Up Period

	Post-Treatment Follow-up Period									
	Procedure	**Post-Procedure**	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total**
Number of Subjects	50	48	45	45	42	22	1	0	0	50
Number of Subjects with Imaging Evaluation	50	41	43	39	39	20	0	-	-	50
Any Minor Device Event	3(6.0%)	0(0.0%)	3(7.0%)	1(2.6%)	0(0.0%)	0(0.0%)	-	-	-	7(14.0%)
Stent Graft Endoleak[1]	0(0.0%)	-	2(4.7%)	1(2.6%)	-	-	-	-	-	3(6.0%)
Stent-graft endoleak type II	-	-	2(4.7%)	1(2.6%)	-	-	-	-	-	3(6.0%)
Device placement at incorrect location	3(6.0%)	-	0(0.0%)	0(0.0%)	-	-	-	-	-	3(6.0%)
Retrograde aortic dissection	0(0.0%)	-	1(2.3%)	0(0.0%)	-	-	-	-	-	1(2.0%)

Note: Percentages are based on the number of subjects with imaging evaluation in the given window.
Study period definitions: Procedure(0-0 days) Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)
MedDRA Version: V15.1
[1] Endoleaks are only reported in the time interval in which the event was first observed. The sum of the type of endoleaks may add up to more than the number of subjects with endoleaks, for subjects can have multiple types

Additional Device Implants

A total of six subjects (6/50, 12%) received an additional stent graft implant following the original procedure as seen in **Table 46**. The CEC adjudication for dissection relatedness is included below and shows that four of the additional device implants were not considered dissection-based by the CEC. Only events

considered related to aortic rupture or malperfusion were previously identified as dissection-based in **Table 41**. Excluding the additional TAG Device implant for subject 0801-135-001 which was conducted as part of a life-saving procedure, all of the cases involved continued false lumen pressurization demonstrated by persistent flow or diameter expansion of the false lumen. These results suggest that a certain portion of the dissection population require treatment greater than exclusion of the primary entry tear that may involve treatment of fenestrations in other parts of the aorta. It also emphasizes the need and importance of follow-up evaluations.

Table 46. Summary of Additional Device Implants

Subject Number	Day of Intervention	Device Used/Technique	Reason for Intervention	CEC Adjudication of Dissection Relatedness
0801-118-002	POD 2	CTAG Device / Standard	Open distal fenestration resulting in persistent flow in false lumen	Related to aortic rupture
0801-120-006	POD 238	CTAG Device / Standard	Type II endoleak, Type 1A endoleak, Enlarging false lumen	Unrelated to malperfusion or aortic rupture
0801-134-001	POD 861	Abdominal Stent Graft	Enlarging distal thoracic aorta due to persistent false lumen flow	Not reviewed by CEC (occurred after 1 year)
0801-135-001	POD 0	TAG Device / Chimney	Retrograde Dissection	Unrelated to malperfusion or aortic rupture
0801-306-001	POD 49	CTAG Device / Standard	Flow in false lumen	Unrelated to malperfusion or aortic rupture
0801-312-001	POD 156	TAG Device / Abdominal Debranching	Expanding descending thoracic aortic aneurysm requiring repair	Unrelated to malperfusion or aortic rupture

Open Intervention

One subject during the course of the study underwent an open repair of the aorta consisting of a surgical graft implanted to supplement the previously placed CTAG Device (**Table 47**). This was considered an additional dissection-based intervention and characterized as "Other treatment or procedure" by the site as previously identified in **Table 41**.

Table 47. Open Surgical Aortic Interventions

Subject Number	Day of Intervention	Reason for Intervention
0801-112-005	POD 676	Enlarging Thoracoabdominal Aorta

Surgical Conversions

No conversions to open surgery were reported.

True and False Lumen Diameter Over Time

Site reported radiological data were used to assess any changes in the true and false lumen diameter over the entire length of the dissected aorta at each time point. As expected in the setting of acute dissection, the true lumen increases and the false lumen decreases following implantation of the CTAG Device. Diameters for both the true and false lumens, for all subjects, are graphed over the

span of 24 months in **Figure 4**. Diameter measurements were performed by the clinical sites due to the potential lack of availability of the software needed to perform area measurements. Supporting data for the graph are located in **Table 48**.

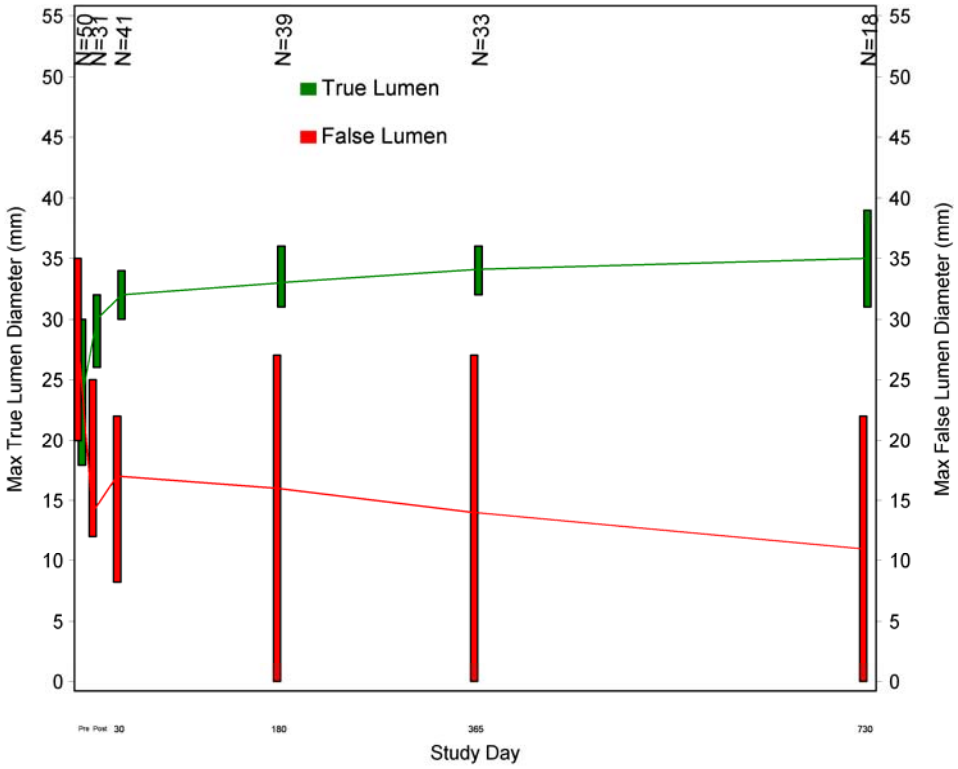

Figure 4. Site Reported True and False Lumen Diameter over Time

Table 48. Summary of True and False Lumen Diameters over Time (Site Reported)_

		Maximum True Lumen Diameter in the DTA		Maximum False Lumen Diameter in the DTA	
Visit	**Statistics**	**Values**	**Change from Pre-Treatment**	**Values**	**Change from Pre-Treatment**
Pre-Treatment	n	50	-	50	-
	Mean (Std Dev)	24.5(8.9)	-	28.0(8.5)	-
	Median	23.5	-	28.5	-
	Range	(8.0,58.0)	-	(12.0,45.0)	-
Post-Procedure	n1	31	31	31	31
	Mean (Std Dev)	29.3(4.9)	3.5(9.3)	18.8(11.5)	-9.5(12.9)
	Median	30.0	4.3	14.0	-7.0
	Range	(15.0,38.0)	(-37.0,14.0)	(0.0,48.0)	(-31.0,17.0)
1 Month	n	41	41	41	41
	Mean (Std Dev)	31.0(6.0)	6.7(8.7)	16.9(10.9)	-10.4(11.9)
	Median	32.0	7.0	17.0	-10.0
	Range	(7.0,41.0)	(-26.0,19.1)	(0.0,46.0)	(-35.0,13.2)

		Maximum True Lumen Diameter in the DTA		Maximum False Lumen Diameter in the DTA	
Visit	**Statistics**	**Values**	**Change from Pre-Treatment**	**Values**	**Change from Pre-Treatment**
6 Months	n	39	39	38	38
	Mean (Std Dev)	33.0(5.9)	9.2(8.6)	15.1(14.0)	-11.7(14.8)
	Median	33.0	11.0	16.0	-14.8
	Range	(7.0,41.0)	(-19.0,21.1)	(0.0,40.0)	(-40.0,14.0)
12 Months	n	33	33	33	33
	Mean (Std Dev)	34.1(5.8)	10.9(9.7)	14.2(13.3)	-11.4(12.7)
	Median	34.1	13.0	14.0	-15.8
	Range	(15.0,51.0)	(-21.0,33.0)	(0.0,36.0)	(-34.0,12.0)
24 Months	n	18	18	17	17
	Mean (Std Dev)	33.9(8.1)	9.9(9.9)	13.2(14.5)	-12.8(14.8)
	Median	35.0	12.5	11.0	-18.0
	Range	(9.0,44.0)	(-14.0,23.1)	(0.0,51.0)	(-34.0,31.0)

Study period definitions: Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days)
MedDRA Version: V15.1
If multiple observations are contained within a single study window, the observation closest to the visit window date is used.
[1] Subjects must have a baseline (Pre-Treatment) and a post-baseline measurement to be available for evaluation.

Core Lab Findings

An independent imaging Core Lab was utilized to assess CT and radiograph images collected for the study. Analysis of study imaging was conducted on both pre- and post-treatment image evaluations. Core Lab assessments included:

- characteristics of access vessels and aortic branches;
- morphology of aortic lesions, adjacent aorta, and landing zones;
- device status (post-implant only); and
- device related issues (post-implant only).

Tables 49, 50, and **51** provide the Core Lab findings. There were no fractures, extrusions/erosions, lumen obstructions, device compressions or thrombi in Core Lab data. The Core Lab identified eleven subjects with an endoleak observed in at least one follow-up period. Three subjects had post-procedural endoleaks prior to the 1 month window that were no longer observed at 1 month without intervention and are not included in **Table 49**, nor discussed in this section. Of the eight subjects with endoleak, only one subject had a Type I endoleak. Seven subjects experienced Type II endoleak. In order to further characterize the observed Type II endoleaks, the sponsor requested the Core Lab to evaluate the point of origination for these endoleaks and a summary of these results are described in **Table 50.** Of the seven subjects who were observed to have a Type II endoleak by the Core Lab, slightly over half of the endoleaks were attributed to an intercostal artery feeding directly into the false lumen. The remaining Type II endoleaks were divided among subjects with a covered left subclavian artery and one subject with differing observations at different time points.

Three subjects (6.7%) with available post-operative imaging had a Core Lab observed device migration at any time point (**Table 51**). Two events were associated with movement of a singular device with the other event as an intercomponent migration. There were no clinical sequelae or interventions related to these findings.

Table 49. Summary of Post-Procedural Core Lab Findings

	Post-Treatment Follow-up Period							
	1 Month	6 Months	12 Months	24 Months	36 Months	48 Months	60 Months	Total Subjects[1]
Number of Subjects	45	45	42	22	1	0	0	45
Number of Subjects With CT/MR Scan[2]	41	39	39	20	0	-	-	44
Number of Subjects With CT/MR or X-Ray[3]	43	39	39	20	0	-	-	45
Endoleak[4]	3 (7.3%)	5 (12.8%)	4 (10.3%)	4 (20.0%)	0(0.0%)	-	-	8 (18.2%)
Type I	1 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-	-	1 (2.3%)
Type II	1 (2.4%)	5 (12.8%)	4 (10.3%)	4 (20.0%)	-	-	-	7 (15.9%)
Indeterminate	1 (2.4%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	-	-	-	2 (4.5%)
Aortic Rupture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
DTA Rupture	-	-	-	-	-	-	-	0 (0.0%)
AAA Rupture	-	-	-	-	-	-	-	0 (0.0%)
Fracture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Extrusion/Erosion	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Lumen Obstruction	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Device Compression	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Thrombus	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)

Study period definitions: 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days) Total(15-2006 days)

[1] The total column represents the number of subjects with any Core Lab reported event during the study. Events reported in multiple follow-up periods for the same subject are counted once in the total column, so the number of events in the rows of the table may not add up to the number of subjects with that event in the total column.

[2] Denominator used in calculation of percentages for events except Fracture

[3] Denominator used in calculation of percentages for Fracture

4 Endoleaks are reported in each time interval in which an event was observed. The sum of the type of endoleaks may add up to more than the number of subjects with endoleaks, for subjects can have multiple types.

Table 50. Core Lab Description of Type II Endoleaks

Origin of Type II Endoleak	Number of Subjects
Type II Endoleak at any time point	7
Intercostal artery supplying false lumen	4 (57.1%)
Covered left subclavian artery	2 (28.6%)
Combination of the two at different time points	1 (14.3%)

Table 51. Summary of Post-Procedural Core Lab Migration Findings

	Post-Treatment Follow-up Period							
	1 Month	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total**
Number of Subjects	45	45	42	22	1	0	0	45
Number of Subjects With CT/MR or X-Ray[1]	43	39	39	20	0	-	-	45
Number of Subjects With CT/MR or X-Ray and >1 Device Implanted[2]	18	17	17	10	0	-	-	20
Migration	1 (2.3%)	0 (0.0%)	3 (7.7%)	1 (5.0%)	0(0.0%)	-	-	3 (6.7%)
Prosthesis Migration	0 (0.0%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0(0.0%)	-	-	2 (4.4%)
Intercomponent Migration	1 (5.6%)	0 (0.0%)	1 (5.9%)	1 (10.0%)	0 (0.0%)	-	-	1 (5.0%)

[1] Denominator used in calculation of percentages for Migration and Prosthesis Migration
[2] Denominator used in calculation of percentages for Intercomponent Migration
Study period definitions: 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days) Total(15-2006 days)

Aortic Morphological Changes - Core Lab

Core Lab reported radiological data were used to assess any changes in the true and false lumen area within the dissected thoracic aorta at each time point. As expected in the setting of acute dissection, the true lumen increases and the false lumen decreases following implantation of the CTAG Device. Areas for both the true and false lumens, for all subjects, are graphed over the span of 24 months in **Figure 5**. Area measurements were performed by the Core Lab because area has the potential to be more sensitive to aortic remodeling than diameter measurements. The selected area measurements were illustrative of the goals of endovascular dissection treatment: expansion of the true lumen and stabilization of the false lumen. Minimum true lumen area and maximum false lumen area were chosen to represent worst-case scenarios, which can lead to differences in results from the site-reported lumen diameter measurements. Supporting data for the graph are located in **Table 52**.

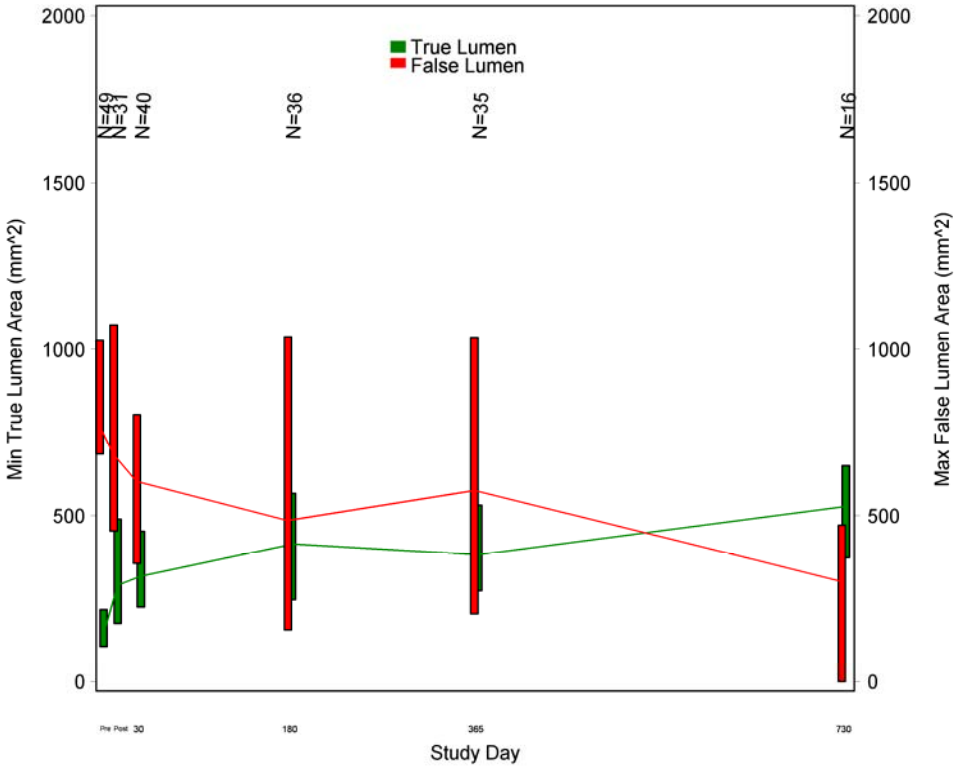

Figure 5. Core Lab Reported True and False Lumen Area over Time

Table 52. Summary of True and False Lumen Areas in the DTA Assessed by the Core Lab

		Minimum True Lumen Area in the DTA		Maximum False Lumen Area in the DTA	
Visit	**Statistics**	**Values**	**Change from Pre-Treatment**	**Values**	**Change from Pre-Treatment**
Pre-Treatment	n	49	-	49	-
	Mean (Std Dev)	218.1(277.3)	-	904.2(387.1)	-
	Median	144.3	-	770.0	-
	Range	(15.8,1884)	-	(185.0,2429)	-
Post-Procedure	n[1]	31	31	31	31
	Mean (Std Dev)	345.6(198.2)	185.0(181.6)	754.4(358.8)	-186(410.5)
	Median	289.1	134.1	683.3	-185
	Range	(73.3,762.6)	(-103,649.8)	(212.2,1679)	(-1746,703.0)
1 Month	n	40	39	40	39
	Mean (Std Dev)	339.7(159.3)	155.3(164.3)	672.9(418.7)	-218(553.6)
	Median	316.7	112.8	602.2	-155
	Range	(58.5,655.8)	(-182,501.1)	(116.5,1705)	(-2222,1040)
6 Months	n	36	35	35	34
	Mean (Std Dev)	412.7(194.3)	220.4(197.7)	635.4(585.0)	-244(608.8)
	Median	413.2	160.4	484.4	-328
	Range	(90.1,762.3)	(-90.0,632.3)	(0.0,2345)	(-1537,1171)

		Minimum True Lumen Area in the DTA		Maximum False Lumen Area in the DTA	
Visit	**Statistics**	**Values**	**Change from Pre-Treatment**	**Values**	**Change from Pre-Treatment**
12 Months	n	35	34	33	32
	Mean (Std Dev)	398.2(167.7)	164.8(321.4)	619.2(489.5)	-242(532.9)
	Median	380.9	179.8	575.5	-154
	Range	(118.1,779.4)	(-1353,631.5)	(0.0,1527)	(-1537,600.6)
24 Months	n	16	15	16	15
	Mean (Std Dev)	518.5(153.8)	191.5(399.2)	448.1(577.7)	-476(573.5)
	Median	527.3	255.4	300.4	-641
	Range	(306.8,789.1)	(-1118,641.2)	(0.0,1882)	(-1537,955.4)

Study period definitions: Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days)
MedDRA Version: V15.1
If multiple observations are contained within a single study window, the observation closest to the visit window date is used.
[1]Subjects must have a baseline (Pre-Treatment) and a post-baseline measurement to be available for evaluation.

Table 53 and **Table 54** show the change in maximum overall aortic diameter in the treated and dissected aorta, respectively (as measured in the axial view). Increase in the aortic diameter over time is more frequently observed in the dissected aorta, suggesting aortic enlargement occurred distal to the stent graft.

Table 53. Change in Overall Aortic Diameter in Treated Segment (Core Lab)

	1 Month	6 Months	12 Months	24 Months
Number of Subjects with Available Data[1]	40	37	36	17
Change in Aortic Diameter from Baseline				
≥ 5mm Decrease	5 (12.5%)	11 (29.7%)	12 (33.3%)	7 (41.2%)
No Change	30 (75.0%)	18 (48.7%)	20 (55.6%)	8 (47.1%)
≥ 5mm Increase	5 (12.5%)	8 (21.6%)	4 (11.1%)	2 (11.8%)

Study period definitions: Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)
If multiple observations are contained within a single study window, the best-case observation (eg. decrease) is used.
[1] Subjects must have a baseline(pre-tx) and a post-baseline measurement to be available for evaluation.

Table 54. Change in Overall Aortic Diameter in Entire Dissected Aorta (Core Lab)

	1 Month	6 Months	12 Months	24 Months
Number of Subjects with Available Data[1]	40	37	36	17
Change in Aortic Diameter from Baseline				
≥ 5mm Decrease	4 (10.0%)	9 (24.3%)	8 (22.2%)	5 (29.4%)
No Change	25 (62.5%)	16 (43.2%)	20 (55.6%)	9 (52.9%)
≥ 5mm Increase	11 (27.5%)	12 (32.4%)	8 (22.2%)	3 (17.7%)

Study period definitions: Post-Procedure(1-14 days) 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)
If multiple observations are contained within a single study window, the best-case observation (eg. decrease) is used.
[1] Subjects must have a baseline(pre-tx) and a post-baseline measurement to be available for evaluation.

Table 55 lists all Core Lab observed device-related events by follow-up period. The only device-related events observed by Core Lab were endoleaks. There were eight subjects with an endoleak observed in at least one follow-up period beginning at 1 month. The Core Lab does not establish whether an endoleak is new or ongoing in their observations. For this reason, it cannot be determined if the endoleaks have resolved or not. It can however be noted which subjects had endoleaks observed in their most recent available follow-up imaging. Two of the eight subjects did not have an endoleak observed on the most recent available follow-up imaging. The remaining six subjects had continued observation of endoleaks on their most recent available follow-up imaging. Three of the seven subjects with Core Lab observed Type II endoleaks had reinterventions completed. The remaining subjects have not had reinterventions associated with the observed endoleaks.

Table 55. Subjects with Device-Related Events by Follow-Up Periods (Core Lab)

	Post-Treatment Follow-up Period							
	1 Month	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total[1]**
Number of Subjects	45	45	42	22	1	0	0	45
Number of Subjects With CT/MR Scan[2]	41	39	39	20	0	-	-	44
Number of Subjects With CT/MR or X-Ray[3]	43	39	39	20	0	-	-	45
Endoleak[4]	3 (7.3%)	5 (12.8%)	4 (10.3%)	4 (20.0%)	0(0.0%)	-	-	8 (18.2%)
Type I	1 (2.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-	-	1 (2.3%)
Type II	1 (2.4%)	5 (12.8%)	4 (10.3%)	4 (20.0%)	-	-	-	7 (15.9%)
Indeterminate	1 (2.4%)	0 (0.0%)	0 (0.0%)	1 (5.0%)	-	-	-	2 (4.5%)
Aortic Rupture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
DTA Rupture	-	-	-	-	-	-	-	0 (0.0%)
AAA Rupture	-	-	-	-	-	-	-	0 (0.0%)
Fracture	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Extrusion/Erosion	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Lumen Obstruction	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Device Compression	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Thrombus	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)
Other	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0(0.0%)	-	-	0 (0.0%)

[1] The total column represents the number of subjects with any Core Lab reported event during the study. Events reported in multiple follow-up periods for the same subject are counted once in the total column, so the number of events in the rows of the table may not add up to the number of subjects with that event in the total column.
[2] Denominator used in calculation of percentages for events except Fracture
[3] Denominator used in calculation of percentages for Fracture
[4] Endoleaks are reported in each time interval in which an event was observed. The sum of the type of endoleaks may add up to more than the number of subjects with endoleaks, for subjects can have multiple types

There were no migrations in the site reported data. Three subjects had a Core Lab observed migrations ≥ 10mm (**Table 56**) at any follow-up time. Two subjects had a Core Lab assessed migration of a single device and one subject had a Core Lab assessed intercomponent migration; none of the observed migrations were associated with clinical sequelae or intervention.

Table 56. Subjects with Migrations by Follow-Up Periods (Core Lab)

	Post-Treatment Follow-up Period							
	1 Month	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**	**Total[1]**
Number of Subjects	45	45	42	22	1	0	0	45
Number of Subjects With CT/MR or X-Ray[2]	43	39	39	20	0	-	-	45
Number of Subjects With CT/MR or X-Ray and >1 Device Implanted[3]	18	17	17	10	0	-	-	20
Migration	1 (2.3%)	0 (0.0%)	3 (7.7%)	1 (5.0%)	0(0.0%)	-	-	3 (6.7%)
Prosthesis Migration	0 (0.0%)	0 (0.0%)	2 (5.1%)	0 (0.0%)	0(0.0%)	-	-	2 (4.4%)
Intercomponent Migration	1 (5.6%)	0 (0.0%)	1 (5.9%)	1 (10.0%)	0 (0.0%)	-	-	1 (5.0%)

Study period definitions: 1 Month(15-59 days) 6 Months(60-242 days) 12 Months(243-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days) Total(15-2006 days)

[1] The total column represents the number of subjects with any Core Lab reported event during the study. Events reported in multiple follow-up periods for the same subject are counted once in the total column, so the number of events in the rows of the table may not add up to the number of subjects with that event in the total column.

[2] Denominator used in calculation of percentages for Migration and Prosthesis Migration

[3] Denominator used in calculation of percentages for Intercomponent Migration

Effectiveness Discussion

One of the goals of treatment in acute complicated Type B dissection is depressurization and reduction of the false lumen with corresponding expansion of the true lumen. Depressurization of the false lumen is accomplished by full exclusion, or coverage, of the primary entry tear that acts as the primary inlet of arterial blood flow into the false lumen. Ideally, coverage of the primary entry tear can lead to false lumen thrombosis and restoration of perfusion to compromised aortic branch vessels.

Data collected in TAG 08-01 demonstrate the following:

- The primary endpoint, exclusion of the primary entry tear of the aortic dissection, was met in 97.5% of assessable subjects at the 1 month visit. This was consistent with historical information provided in the TAG 08-01 protocol.

- Based on the last available follow-up, 93.3% of the subjects experienced some degree of false lumen thrombosis with 73.3% of subjects experiencing complete false lumen thrombosis. These results are consistent with historical information provided in the TAG 08-01 protocol.
- Additional dissection-based interventions were performed in a total of 14% of the study subjects. This is lower than historical results presented in the TAG 08-01 protocol, although the information in the protocol was excerpted from scientific literature that may have used different definitions.
- There was an observed rupture rate of 4% in the study that is consistent with the medical literature.
- Investigational sites did not report any device events from the categories of fracture, extrusion/erosion, lumen obstruction, device compression or thrombus. The Core Lab confirmed that none of these device events had occurred.
- The Core Lab identified one subject who experienced intercomponent device migration. There were two Core Lab observed single prosthesis migrations. None of the migration events were reported by the site nor were they related to adverse events or treatments.
- Aortic remodeling data were positive from the site and Core Lab assessments, demonstrating general increases in the true lumen and decreases in the false lumen as expected.

The results of the TAG 08-01 clinical trial suggest that the CTAG Device is an effective treatment option for coverage of the primary entry tear of acute complicated Type B aortic dissection. Depending on the patient's condition, adjunctive procedures and/or devices may be required to complete the treatment of the dissection.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 214 of which none were full-time or part-time employees of the sponsor and 13 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: 13
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

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.

XI. Summary of Supplemental Clinical Information on Acute Type B Aortic Dissection

A. TAG 04-01 Acute DTA Complex Aortic Pathologies Feasibility Study - Design and Result Summary

TAG 04-01 was a multi-center study planned to evaluate the safety and effectiveness of stent graft treatments for complex thoracic pathologies including acute complicated Type B aortic dissection. Fifty-nine (59) subjects were enrolled into the TAG 04-01 study at 14 investigative sites between August 2005 and February 2007. Subjects were enrolled in three study arms based on the DTA pathology; acute complicated distal dissection (n = 19), traumatic transection (n = 20) and aneurysm rupture (n = 20). Subjects were assessed at pre-treatment, treatment, and hospital discharge and returned for follow-up visits at 1 month, 6 months and annually thereafter. Subjects were followed for 5 years post-treatment.

The primary endpoint for this clinical study was the short-term composite outcome of death and paraplegia in subjects treated with the TAG Device for complex pathology of the DTA. Short-term subject mortality was defined as death of any cause ≤ 30 days post-treatment. Motor function was assessed with a standardized scale when the subject emerged from anesthesia post-treatment, at hospital discharge, and at the 30 day follow-up visit. Mortality in the TAG 04-01 subjects through 30 days was 15.8% (3/19) in the acute complicated Type B dissection cohort.

Table 57 summarizes all major adverse events (MAEs) reported during the conduct of the TAG 04-01 study for the dissection cohort.

Table 57. Summary of Major Adverse Events (MAEs) by Study Interval

	Post-Treatment Follow-up Period						
Acute Complicated Dissection	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**
Evaluable Subjects[1]	19	15	15	14	14	10	8
Subjects With One or More Major Adverse Events	14(73.7%)	5(33.3%)	4(26.7%)	5(35.7%)	3(21.4%)	3(30.0%)	2(25.0%)
Vascular disorders	6(31.6%)	1(6.7%)	3(20.0%)	3(21.4%)	1(7.1%)	0(0.0%)	1(12.5%)
Aneurysms and dissections non-site specific	2(10.5%)	0(0.0%)	1(6.7%)	1(7.1%)	0(0.0%)	-	0(0.0%)
Aneurysm	1(5.3%)	-	0(0.0%)	1(7.1%)	-	-	-
Aneurysm ruptured	1(5.3%)	-	0(0.0%)	0(0.0%)	-	-	-
Artery dissection	0(0.0%)	-	1(6.7%)	0(0.0%)	-	-	-
Aortic aneurysms and dissections	2(10.5%)	1(6.7%)	1(6.7%)	0(0.0%)	0(0.0%)	-	1(12.5%)
Aortic dissection	1(5.3%)	1(6.7%)	1(6.7%)	-	-	-	1(12.5%)
Aortic aneurysm	1(5.3%)	0(0.0%)	0(0.0%)	-	-	-	0(0.0%)
Peripheral embolism and thrombosis	1(5.3%)	0(0.0%)	0(0.0%)	1(7.1%)	1(7.1%)	-	0(0.0%)
Deep vein thrombosis	1(5.3%)	-	-	1(7.1%)	1(7.1%)	-	-
Non-site specific vascular disorders NEC	2(10.5%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	-	0(0.0%)
Haemodynamic instability	2(10.5%)	-	-	-	-	-	-
Peripheral vasoconstriction, necrosis and vascular insufficiency	1(5.3%)	0(0.0%)	1(6.7%)	0(0.0%)	0(0.0%)	-	0(0.0%)
Intermittent claudication	0(0.0%)	-	1(6.7%)	-	-	-	-
Peripheral ischaemia	1(5.3%)	-	0(0.0%)	-	-	-	-
Site specific vascular disorders NEC	1(5.3%)	0(0.0%)	1(6.7%)	0(0.0%)	0(0.0%)	-	0(0.0%)
Aortic rupture	1(5.3%)	-	1(6.7%)	-	-	-	-
Vascular hypertensive disorders NEC	1(5.3%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	-	0(0.0%)
Hypertension	1(5.3%)	-	-	1(7.1%)	-	-	-
Vascular hypotensive disorders	1(5.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	-	0(0.0%)
Hypotension	1(5.3%)	-	-	-	-	-	-
Cardiac disorders	3(15.8%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)	1(12.5%)
Ischaemic coronary artery disorders	1(5.3%)	-	-	0(0.0%)	-	-	1(12.5%)
Angina pectoris	1(5.3%)	-	-	-	-	-	1(12.5%)
Coronary artery disorders NEC	0(0.0%)	-	-	1(7.1%)	-	-	0(0.0%)
Coronary artery disease	-	-	-	1(7.1%)	-	-	-
Rate and rhythm disorders NEC	1(5.3%)	-	-	0(0.0%)	-	-	0(0.0%)
Bradycardia	1(5.3%)	-	-	-	-	-	-
Ventricular arrhythmias and cardiac arrest	1(5.3%)	-	-	0(0.0%)	-	-	0(0.0%)
Cardiac arrest	1(5.3%)	-	-	-	-	-	-
Nervous system disorders	5(26.3%)	0(0.0%)	0(0.0%)	2(14.3%)	0(0.0%)	0(0.0%)	0(0.0%)
Central nervous system haemorrhages and cerebrovascular accidents	4(21.1%)	-	-	1(7.1%)	-	-	-
Cerebrovascular accident	3(15.8%)	-	-	0(0.0%)	-	-	-
Brain stem infarction	1(5.3%)	-	-	0(0.0%)	-	-	-
Cerebral haemorrhage	0(0.0%)	-	-	1(7.1%)	-	-	-
Central nervous system vascular disorders NEC	0(0.0%)	-	-	1(7.1%)	-	-	-
Carotid artery stenosis	-	-	-	1(7.1%)	-	-	-
Paraesthesias and dysaesthesias	1(5.3%)	-	-	0(0.0%)	-	-	-
Burning sensation	1(5.3%)	-	-	-	-	-	-
Paraesthesia	1(5.3%)	-	-	-	-	-	-
Paralysis and paresis (excl cranial nerve)	1(5.3%)	-	-	0(0.0%)	-	-	-
Paraparesis	1(5.3%)	-	-	-	-	-	-
General disorders and administration site conditions	4(21.1%)	0(0.0%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)
Vascular complications associated with device	2(10.5%)	-	-	-	0(0.0%)	-	-
Stent-graft endoleak	2(10.5%)	-	-	-	-	-	-
Asthenic conditions	1(5.3%)	-	-	-	0(0.0%)	-	-

	Post-Treatment Follow-up Period						
Acute Complicated Dissection	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**
Asthenia	1(5.3%)	-	-	-	-	-	-
Death and sudden death	0(0.0%)	-	-	-	1(7.1%)	-	-
Death	-	-	-	-	1(7.1%)	-	-
Pain and discomfort NEC	1(5.3%)	-	-	-	0(0.0%)	-	-
Chest discomfort	1(5.3%)	-	-	-	-	-	-
Renal and urinary disorders	3(15.8%)	1(6.7%)	1(6.7%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Renal failure and impairment	2(10.5%)	0(0.0%)	1(6.7%)	-	-	-	-
Renal failure	2(10.5%)	-	0(0.0%)	-	-	-	-
Renal failure acute	0(0.0%)	-	1(6.7%)	-	-	-	-
Renal vascular and ischaemic conditions	0(0.0%)	1(6.7%)	0(0.0%)	-	-	-	-
Renal artery stenosis	-	1(6.7%)	-	-	-	-	-
Urethral disorders NEC	1(5.3%)	0(0.0%)	0(0.0%)	-	-	-	-
Urethral discharge	1(5.3%)	-	-	-	-	-	-
Respiratory, thoracic and mediastinal disorders	5(26.3%)	0(0.0%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)
Breathing abnormalities	2(10.5%)	-	-	-	0(0.0%)	-	-
Dyspnoea	1(5.3%)	-	-	-	-	-	-
Respiratory arrest	1(5.3%)	-	-	-	-	-	-
Respiratory failures (excl neonatal)	2(10.5%)	-	-	-	0(0.0%)	-	-
Respiratory failure	2(10.5%)	-	-	-	-	-	-
Coughing and associated symptoms	1(5.3%)	-	-	-	0(0.0%)	-	-
Haemoptysis	1(5.3%)	-	-	-	-	-	-
Pneumothorax and pleural effusions NEC	1(5.3%)	-	-	-	0(0.0%)	-	-
Pneumothorax	1(5.3%)	-	-	-	-	-	-
Pulmonary thrombotic and embolic conditions	0(0.0%)	-	-	-	1(7.1%)	-	-
Pulmonary embolism	-	-	-	-	1(7.1%)	-	-
Infections and infestations	1(5.3%)	1(6.7%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	1(12.5%)
Abdominal and gastrointestinal infections	0(0.0%)	1(6.7%)	-	-	0(0.0%)	-	0(0.0%)
Appendiceal abscess	-	1(6.7%)	-	-	-	-	-
Bone and joint infections	0(0.0%)	0(0.0%)	-	-	0(0.0%)	-	1(12.5%)
Arthritis infective	-	-	-	-	-	-	1(12.5%)
Lower respiratory tract and lung infections	0(0.0%)	0(0.0%)	-	-	1(7.1%)	-	0(0.0%)
Pneumonia	-	-	-	-	1(7.1%)	-	-
Retroviral infections	1(5.3%)	0(0.0%)	-	-	0(0.0%)	-	0(0.0%)
Retroviral infection	1(5.3%)	-	-	-	-	-	-
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)
Non-small cell neoplasms malignant of the respiratory tract cell type specified	-	-	-	-	1(7.1%)	-	-
Lung squamous cell carcinoma stage unspecified	-	-	-	-	1(7.1%)	-	-
Blood and lymphatic system disorders	1(5.3%)	1(6.7%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Anaemias NEC	0(0.0%)	1(6.7%)	-	-	-	-	-
Anaemia	-	1(6.7%)	-	-	-	-	-
Coagulopathies	1(5.3%)	0(0.0%)	-	-	-	-	-
Coagulopathy	1(5.3%)	-	-	-	-	-	-
Psychiatric disorders	1(5.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Mental disorders NEC	1(5.3%)	-	-	-	-	-	-
Mental status changes	1(5.3%)	-	-	-	-	-	-
Eye disorders	1(5.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Ocular nerve and muscle disorders	1(5.3%)	-	-	-	-	-	-
Eye movement disorder	1(5.3%)	-	-	-	-	-	-
Gastrointestinal disorders	0(0.0%)	1(6.7%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)	0(0.0%)
Gastrointestinal signs and symptoms NEC	-	0(0.0%)	-	1(7.1%)	-	-	-

	Post-Treatment Follow-up Period						
Acute Complicated Dissection	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**
Dysphagia	-	-	-	1(7.1%)	-	-	-
Non-site specific gastrointestinal haemorrhages	-	1(6.7%)	-	0(0.0%)	-	-	-
Gastrointestinal haemorrhage	-	1(6.7%)	-	-	-	-	-
Hepatobiliary disorders	0(0.0%)	0(0.0%)	1(6.7%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Hepatic failure and associated disorders	-	-	1(6.7%)	-	-	-	-
Hepatic failure	-	-	1(6.7%)	-	-	-	-
Skin and subcutaneous tissue disorders	0(0.0%)	1(6.7%)	0(0.0%)	1(7.1%)	0(0.0%)	0(0.0%)	0(0.0%)
Connective tissue disorders	-	0(0.0%)	-	1(7.1%)	-	-	-
Nephrogenic systemic fibrosis	-	-	-	1(7.1%)	-	-	-
Skin ischaemic conditions	-	1(6.7%)	-	0(0.0%)	-	-	-
Dry gangrene	-	1(6.7%)	-	-	-	-	-
Musculoskeletal and connective tissue disorders	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	1(10.0%)	1(12.5%)
Osteoarthropathies	-	-	-	-	-	1(10.0%)	1(12.5%)
Osteoarthritis	-	-	-	-	-	1(10.0%)	1(12.5%)
Reproductive system and breast disorders	1(5.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Scrotal disorders NEC	1(5.3%)	-	-	-	-	-	-
Scrotal oedema	1(5.3%)	-	-	-	-	-	-
Investigations	1(5.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Red blood cell analyses	1(5.3%)	-	-	-	-	-	-
Haematocrit decreased	1(5.3%)	-	-	-	-	-	-
Injury, poisoning and procedural complications	3(15.8%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Non-site specific procedural complications	1(5.3%)	-	-	-	-	-	-
Post procedural haemorrhage	1(5.3%)	-	-	-	-	-	-
Poisoning and toxicity	1(5.3%)	-	-	-	-	-	-
Toxicity to various agents	1(5.3%)	-	-	-	-	-	-
Respiratory tract and thoracic cavity procedural complications	1(5.3%)	-	-	-	-	-	-
Endotracheal intubation complication	1(5.3%)	-	-	-	-	-	-
Surgical and medical procedures	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	2(20.0%)	1(12.5%)
Diaphragmatic therapeutic procedures	-	-	-	-	-	1(10.0%)	0(0.0%)
Hernia hiatus repair	-	-	-	-	-	1(10.0%)	-
Joint therapeutic procedures	-	-	-	-	-	1(10.0%)	1(12.5%)
Hip arthroplasty	-	-	-	-	-	1(10.0%)	1(12.5%)

[1]Subjects are considered evaluable if date of last contact for the subject is on or after the first day of the given time window. The denominators for each entry are the number of evaluable subjects in that time window.
An event with a '-' indicates no subjects reported the event.
Study period definitions: 1 Month(0-60 days) 6 Months(61-304 days) 12 Months(305-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)
Events with onset date prior to study day 0 are recoded to study day 0 for analysis.

Table 58 summarizes all major device events by interval reported during the conduct of the TAG 04-01 study for the dissection cohort. A major device event was experienced by 4 subjects (21.1%) through the 1 month visit and 2 subjects (13.3%) through the 6 month visit. No major device events were reported after 6 months.

Table 58. Summary of Major Device Events by Study Interval

	Post-Treatment Follow-up Period						
Acute Complicated Dissection	**1 Month**	**6 Months**	**12 Months**	**24 Months**	**36 Months**	**48 Months**	**60 Months**
Evaluable Subjects[1]	19	15	15	14	14	10	8
Subjects With One or More Major Device Events	4(21.1%)	2(13.3%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)	0(0.0%)
Vascular disorders	3(15.8%)	1(6.7%)	-	-	-	-	-
Aneurysms and dissections non-site specific	2(10.5%)	0(0.0%)	-	-	-	-	-
Aneurysm	1(5.3%)	-	-	-	-	-	-
Aneurysm ruptured	1(5.3%)	-	-	-	-	-	-
Aortic aneurysms and dissections	0(0.0%)	1(6.7%)	-	-	-	-	-
Aortic dissection	-	1(6.7%)	-	-	-	-	-
Site specific vascular disorders NEC	1(5.3%)	0(0.0%)	-	-	-	-	-
Aortic rupture	1(5.3%)	-	-	-	-	-	-
General disorders and administration site conditions	1(5.3%)	0(0.0%)	-	-	-	-	-
Vascular complications associated with device	1(5.3%)	-	-	-	-	-	-
Stent-graft endoleak	1(5.3%)	-	-	-	-	-	-
Renal and urinary disorders	0(0.0%)	1(6.7%)	-	-	-	-	-
Renal vascular and ischaemic conditions	-	1(6.7%)	-	-	-	-	-
Renal artery stenosis	-	1(6.7%)	-	-	-	-	-

[1]Subjects are considered evaluable if date of last contact for the subject is on or after the first day of the given time window. The denominators for each entry are the number of evaluable subjects in that time window.
An event with a '-' indicates no subjects reported the event.
Study period definitions: 1 Month(0-60 days) 6 Months(61-304 days) 12 Months(305-546 days) 24 Months(547-911 days) 36 Months(912-1275 days) 48 Months(1276-1640 days) 60 Months(1641-2006 days)
Events with onset date prior to study day 0 are recoded to study day 0 for analysis.

Five year follow-up data in the TAG 04-01 acute complicated Type B aortic dissection cohort have provided supportive evidence that the CTAG Device is a safe, effective and durable treatment option in the treatment of acute complicated Type B aortic dissection. Short-term mortality and paraplegia outcomes are reflective of published studies and case series of the treatment of acute complicated Type B aortic dissection using endovascular stent grafts. No unanticipated adverse events were observed through five years of follow-up.

B. Justification for Indication

Diseases or injuries of the descending thoracic aorta can be classified as either isolated lesions or Type B dissections. The CTAG Device is currently approved for the treatment of isolated lesions (excluding dissections) of the descending thoracic aorta (P040043/S40). This PMA supplement expands the indications for use to include treatment of all lesions of the descending thoracic aorta including dissections.

There are two types of Type B dissections: acute and chronic. Acute dissections have historically been defined as dissections that are diagnosed within 14 days of symptom onset. Acute dissections can be sub-divided into complicated and uncomplicated dissections. Acute complicated dissections require intervention in order to resolve emergent complications that cannot be managed with medication alone, such as malperfusion or rupture, while acute uncomplicated dissections are treated in order to resolve less emergent conditions, such as uncontrollable pain, chronic hypertension, or impending rupture. The treatment goal for all acute Type B dissections is to cover the primary entry tear, repressurize and expand the true lumen, and depressurize the false lumen, which promotes false lumen thrombosis in the treated length.

The safety and effectiveness of the CTAG Device for the treatment of acute complicated Type B dissections was established with the TAG 08-01 Dissection Study. Because the CTAG Device was evaluated in a more compromised patient population as compared to patients with uncomplicated dissections and there was no suggestion that the device would be less safe or effective in the uncomplicated population, this information can be extrapolated to address the safety and effectiveness of the broader population of patients with acute dissections.

Chronic dissections have historically been defined as dissections that are diagnosed more than 14 days after symptom onset; chronic dissections started as acute uncomplicated dissections that were medically managed only or untreated. The primary reason for intervention is often aneurysmal dilation of the false lumen (impending rupture), uncontrollable pain, or acute extension of dissection (acute on chronic) leading to acute phase complications such as malperfusion. As aneurysmal dilation of the false lumen is the most common reason for intervention of chronic dissections, the conditions that lead to intervention are often similar to aneurysms. These conditions include a total aortic diameter of ≥ 5.5cm, rapid growth or impending rupture of the false lumen, or a symptomatic aneurysmal false lumen. The treatment goal for chronic Type B dissections is the same as for acute Type B dissections: cover the primary entry tear, repressurize and expand the true lumen, and depressurize the false lumen, which promotes false lumen thrombosis in the treated length. When treating chronic Type B dissections with endovascular devices, many of the considerations during treatment are similar to those of aneurysm patients as well as acute Type B dissection patients, including the risk of endoleaks leading to repressurization of

the false lumen, distal tears allowing continued perfusion of the false lumen, and sufficient length of coverage to optimize exclusion of arterial flow to the lesion. The cumulative data from the TAG 08-03 Aneurysm Study and the TAG 08-01 Dissection Study provide physicians with significant knowledge that will assist with treatment of chronic Type B dissections including IFU warnings and precautions around treatment of these patients generated from the conclusions of these studies. This study data, combined with peer reviewed literature, supplements known safety information regarding the endovascular treatment of chronic Type B dissections. **Table 59** shows a selection of peer reviewed articles with longer-term follow-up on endovascular treatment of patients with chronic Type B dissections. These data are consistent with other published literature on endovascular treatment of chronic Type B dissections and show low peri-operative mortality rates and high mid-term survival rates for this patient population. Reasonable assurance of effectiveness of the treatment of chronic Type B dissections can be inferred from the TAG 08-01 and TAG 08-03 data. In addition, reasonable assurance of safety of the treatment of chronic Type B dissections can be inferred from a combination of the TAG 08-01 and TAG 08-03 data as well as from peer reviewed literature.

Table 59. Literature Review for Endovascular Treatment of Chronic Type B Dissections

Publication	N	Follow-up	Operative Mortality	Mid-term Survival
Mani [26]	58	48 months	5%	57%
Sayer[27]	40	30 months	7.5%	66.5%
Parsa[28]	51	60 months	0	78%
Oberhuber[29]	19	13 months	0	N/A
Manning[30]	10	56 months	0	100%

Data from multiple studies (TAG 97-01, TAG 99-01, TAG 03-03, TAG 06-02 and TAG 08-03) have demonstrated reasonable assurance of safety in the endovascular treatment of descending thoracic aortic aneurysms. The TAG 08-02 Traumatic Transection study extended the assurance of safety to isolated lesions of the descending thoracic aorta; the TAG 04-01 and TAG 08-01 Dissection studies further extended the assurance of safety to include Type B dissections. The data from the combination of these studies, supported and substantiated with peer reviewed literature, demonstrate reasonable assurance of safety in the endovascular treatment of all lesions of the descending thoracic aorta.

Effectiveness of the treatment of aneurysms, traumatic transections, and acute complicated Type B dissections was also established with all of the studies that were completed to demonstrate a reasonable assurance of safety. Given the similarities in reasons for treatment and treatment goals, there is reasonable assurance of effectiveness for the treatment of all other descending thoracic aortic diseases and injuries.

In total, clinical experience has shown that a thoracic stent graft can be safely introduced and delivered in patients with various types of aortic pathologies,

however; some pathologies (e.g., dissection, rupture) carry additional inherent risk. The clinical experience also shows that thoracic stent grafts can perform their intended purpose in a reliable fashion without causing significant detriment to the patient both in the short and mid-term following intervention. A general indication for the treatment of all lesions of the descending thoracic aorta allows physicians to choose endovascular repair with an on-label indication if they feel it is the best option for their patients based on available safety and effectiveness data.

XII. Panel Meeting Recommendation and FDA's Post-Panel Action

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. Conclusions Drawn from Preclinical and Clinical Studies and Supplementary Data

A. Effectiveness Conclusions

The primary effectiveness endpoint of this study was exclusion of the primary entry tear at the 1 month follow-up visit. The percentage of subjects with successful closure of the primary entry tear at 1 month was 97.5% which is within the reported primary entry tear exclusion rates reported in the medical literature (88 – 100%). In addition, exclusion of the entry tear was evaluated at 12 months with a 100% exclusion entry tear rate in available subjects.

Secondary effectiveness endpoints included false lumen thrombosis (assessed by the Core Lab), additional dissection-based intervention and aortic rupture through the course of available follow-up. Median follow-up (procedure to last known contact date) was 497 days. The percentage of complete thrombosis at a level adjacent to the stent graft at the last available follow-up visit is 73.3%. A total of seven subjects (14%) underwent ten procedures following CTAG Device implant that were directly associated with the original, presenting aortic dissection as determined by the CEC or site Investigators. Two events of aortic rupture (4%) were reported by sites over the entire duration of the study. The secondary effectiveness endpoint results of the study are comparable to the results published in the medical literature.

Major device events (n=6, 12%) reported in the study consisted of endoleaks (Type IA and Type II), aortic rupture, complication of device catheter removal, and retrograde aortic dissection.

Six subjects (12%) received additional stent graft implants. With the exception of the subject with an additional TAG Device implanted as part of an attempted life saving procedure, all additional device implants were done in an effort to exclude additional points of arterial inflow into the false lumen through a point other than the primary entry tear. Secondary points of arterial supply to the false lumen can be a contributing factor in the continuation or progression of the dissection disease state. The process can be visualized on a CT scan as persistent flow and/or growth of the false lumen. One potential source of false lumen arterial supply would be a fenestration, distal to the aorta covered by the CTAG Device, providing enough significant blood flow to the false lumen to resist the thrombosis process and dilate the false lumen. A portion of subjects also had their left subclavian artery occluded by embolization coils to eliminate another potential source of endoleak into the false lumen. A large majority of subjects (n=44, 88%) did not require any sort of reintervention making the clinical need for coil embolization of the left subclavian artery or long segment coverage of the descending thoracic aorta up to the discretion of the treating surgeon.

One subject during the course of the study underwent an open repair of the aorta consisting of a sewn graft to supplement the previously placed CTAG Device. No conversions to open surgery were reported.

Aortic remodeling data were positive from the site and Core Lab assessments, demonstrating general increases in the true lumen and decreases in the false lumen as expected.

Investigational sites did not report any device events from the categories of fracture, extrusion/erosion, lumen obstruction, device compression or thrombus. The Core Lab confirmed that none of these device events had occurred. The Core Lab identified one subject who experienced intercomponent device migration. There were two Core Lab observed single prosthesis migrations. None of the migration events were reported by the site nor were they related to adverse events or treatments.

The results of the TAG 08-01 clinical study suggest that the CTAG Device is an effective treatment option for acute complicated Type B aortic dissection.

Information reviewed under separate PMA supplements (P040043/S39 and P040043/S40) provided the additional information needed to support the effectiveness of the broader indication of treatment of the descending thoracic aorta.

B. Safety Conclusions

The risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above.

The primary safety endpoint was all-cause mortality at 30 days. A total of 4 subjects died within 30 days post-procedure. One additional subject was unable to be located or contacted after leaving the hospital and was considered non-responder (as per protocol). Therefore, the posterior probability that the proportion of subjects experiencing 30 day mortality following treatment with the CTAG device for acute complicated Type B dissection is <0.25 is 0.994 which meets the performance goal outlined in the study protocol. Despite the fact that some deaths were related to the endovascular procedure and/or the device, the overall mortality seen in this study is very low. Also, if these patients who died had not been given the option of endovascular repair they likely would have died anyway due to the natural course of this aggressive aortic emergency.

Although the overall incidence of stroke in the present study appears to be high (18%), the vast majority of subjects recovered. One subject had permanent deficit and one subject died. The location of these strokes and their association with proximal aneurysmal disease implicate multiple emboli to the anterior and posterior circulation, arising from the aortic arch, from catheter, guidewire, or device manipulation in a diseased arch. The presence of vertebrobasilar disease or dominant left vertebral may play an important role specially when the LSA is covered by the stent graft and not revascularized. Please note that 7 out of 9 subjects with strokes had the LSA either partially or completely covered and only one of these subjects had the LSA bypassed, which represents in itself a risk factor for stoke. With these considerations in mind, the overall rates of stroke of 18%, with a rate of disabling stroke of 4%, appears to be acceptable for patients presenting with this disease. The rates of disabling strokes after endovascular repair for acute aortic dissection ranges from 0 – 9%.

These results in addition to those reported under PMA supplement (P040043/S39 and P040043/S40) provided the additional information needed to support the safety of the broader indication of treatment of the descending thoracic aorta.

C. Benefit-Risk Conclusions

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above.

Patients diagnosed with descending thoracic aortic dissection are generally managed with a complication-specific approach. Traditionally, dissections associated with no or minimal impact on body systems are treated with a medical regimen focused on strict blood pressure control with the treatment goal to prevent any further progression of the dissection. However, a recent randomized controlled clinical study published in Circulation Cardiovascular Interventions, concluded that the use of aortic endografts in addition to optimal medical therapy was associated with improved 5-years aorta-specific survival and delayed disease progression. Therefore, the use of endografts in stable Type B dissection with suitable anatomy may be considered to improve late outcome.

For patients with significant impact on body systems, also referred as complicated dissections, an intervention is necessary. The types of interventions available for complicated dissections are either open surgical repair, which includes an open thoracotomy that carries significant mortality and morbidity, or endovascular repair.

In the presence of rupture or malperfusion, acute aortic dissection is a real vascular emergency that requires immediate intervention and which has one of the highest mortality rates of the cardiovascular diseases. Conventional open surgical and medical therapies continue to be associated with significant mortality risk which is reported to be as high as 50%. Although open surgery can be performed to repair the dissection entry tear, the operation itself is technically challenging due to the fact that the aortic tissues are very fragile which make it difficult to sew a synthetic graft with adequate anastomosis. Therefore, there are no good alternative treatments for patients presenting with acute complicated Type B aortic dissection.

Patients that survive the acute dissection episode become chronic dissections. Chronic dissections tend to be more like descending thoracic aneurysm in the sense that the indications for interventions are oftentimes related to the size of the aorta. Long-term prognosis of chronic Type B dissection is sobering, with just 60% to 80% survival estimates at 5 years using conservative management because complications and aneurysm expansion are likely. Once the aortic diameter exceeds 5.5 to 6.0 cm, the risk of rupture is estimated at 30% per year. Even if medical therapy is considered the best option for uncomplicated Type B aortic dissection, the effect of medical therapy may delay the expansion of the descending aorta, but would not enhance the remodeling process. Late interventions are often performed in chronic Type B aortic dissection for development of complications, such as aneurysm expansion, progressive/new dissection, and other related adverse events from the unresolved dissection process. Recurrence of symptoms, aneurysmal dilation (total aortic diameter ≥

5.5 cm), or a yearly increase (>4mm) of aortic diameter should be considered signs of instability in the chronic phase and indication for thoracic endovascular repair, or in unsuitable anatomy, indication for open surgery, as the early mortality in complicated chronic Type B aortic dissection is lower with TEVAR compared with open surgery.

Clinical benefit to the acute dissection patient is the immediate restoration of circulation to ischemic tissues or exclusion of an aortic rupture site. Chronic patients will be eligible for a less invasive procedure and enjoy the peri-operative benefits commonly described in a descending aneurysm population. Following endovascular treatment, patients are able to resume their normal daily activities in a more rapid fashion as compared to patients treated with open surgical repair. Stabilized patients can enter a maintenance phase with their follow-up physician concentrating on blood pressure management and serial observation of the dissection for potential continued progression in other parts of the aorta. Residual risks to the patient remain after CTAG Device implant due to the aortic dissection disease process and its potential negative impact on the vascular system. As with all thoracic stent grafts, risks are monitored with serial follow-up evaluations and active physician oversight.

In conclusion, the information presented above and the published medical literature support that the probable benefits outweigh the probable risk for using the CTAG Device for the treatment of aortic dissections and therefore the modification to the current indications for the device.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The safety and effectiveness of the treatment of aneurysms, traumatic transections, and acute complicated Type B dissections with the TAG Device has been established with the previous TAG studies and TAG 08-03, TAG 08-02, and TAG 08-01 studies, respectively. Given the similarities in reasons for treatment and treatment goals, there is reasonable assurance of safety and effectiveness for the treatment all other descending thoracic aortic diseases and injuries.

The addition of the treatment of dissections in the indications for the TAG Device will provide an on-label, less-invasive treatment option for patients. Based on the available data, it can be assumed that patients will benefit from this treatment option, given the low mortality rate observed in the clinical study.

Based on all data presented, the GORE® CTAG Thoracic Endoprosthesis has demonstrated a reasonable assurance of safety and effectiveness in the endovascular repair of the descending thoracic aorta in patients with appropriate

vascular anatomy and who are candidates for endovascular treatment. However, patients who have known sensitivities or allergies to the device materials or who have an infection that presents an increased risk of device infection should not be treated with the device.

XIV. CDRH Decision

CDRH issued an approval order on September 10, 2013. The final conditions of approval are cited in the approval order.

XV. Approval Specifications

Instructions for Use: See device labeling.

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

Post-Approval Requirements and Restrictions: See approval order.

XVI. References

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