

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. General Information

Device Generic Name: Endovascular Graft

Device Trade Name: GORE® TAG® Thoracic Endoprosthesis

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

Date(s) of Panel Recommendation: none

Premarket Approval Application (PMA) Number: P040043/S040

Date of FDA Notice of Approval: 01/13/2012

Expedited: not applicable

The original PMA (P040043) was approved on March 23, 2005 and is intended for endovascular repair of isolated lesions (not including dissections) of the descending thoracic aorta, 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

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to expand the indication for the GORE TAG Thoracic Endoprosthesis.

PMA supplement P040043/S040 was submitted to obtain approval to market the conformable GORE® TAG® Thoracic Endoprosthesis for the endovascular repair of isolated lesions of the descending thoracic aorta (DTA). This supplement P040043/S040 represents a new indication for use for the device. Previously the device was indicated for use in the endovascular repair of aneurysms of the DTA. The data presented below support the use of the device for the treatment of aortic transections. These data, in combination with the data provided previously in this PMA, are adequate to demonstrate that the device is a safe and effective treatment option for an expanded indication for use, that is, isolated lesions of the DTA. This broader indication, which excludes the treatment

of dissections, includes the treatment of all types of isolated lesions in the DTA, such as, saccular and fusiform aneurysms, penetrating ulcers, isolated hematomas, and transections. Because of the significant challenges in conducting a study that would capture data on each of the lesion types, the broader indication is supported by the data for the most challenging lesion type to treat endovascularly (i.e., aneurysms) and the other relatively common isolated lesion treated endovascularly (i.e., transections). 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), as compared to the original PMA device. Please note that 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.

The CTAG Device received premarket approval for the endovascular repair of aneurysms of the descending thoracic aorta via non-panel-track 180-day PMA supplement P040043/S039 on August 23, 2011. Because isolated lesions of the descending thoracic aorta encompass aneurysms, data supporting the safety and effectiveness of the device in the treatment of aneurysms of the descending thoracic aorta that were originally submitted in P040043/S039 are also included here.

II. Indications for Use

The GORE® TAG® Thoracic Endoprosthesis is intended for endovascular repair of isolated lesions (not including dissections) of the descending thoracic aorta, 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

III. Contraindications

The GORE® TAG® Thoracic Endoprosthesis is contraindicated in:

- Patients with known sensitivities or allergies to the device materials
- 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).

V. Device Description

The GORE® TAG® Thoracic Endoprosthesis provides endovascular repair of isolated lesions of the descending thoracic aorta (DTA). The GORE® TAG® Thoracic Endoprosthesis may be used as a single device or in multiple device combinations 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 two parts, the endoprosthesis and the delivery system (**Figures 1 and 2**). Endoprosthesis sizes range in diameter from 21 to 45 mm and in length from 10 to 20 cm (**Table 1**). The compressed profile of these devices on a delivery catheter ranges from 18 to 24 Fr.

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, 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.

The delivery system consists of a catheter and a sewn deployment sleeve. The catheter is compatible with a 0.035" or smaller 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. Pulling the deployment knob, which is attached to the deployment line system, 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.

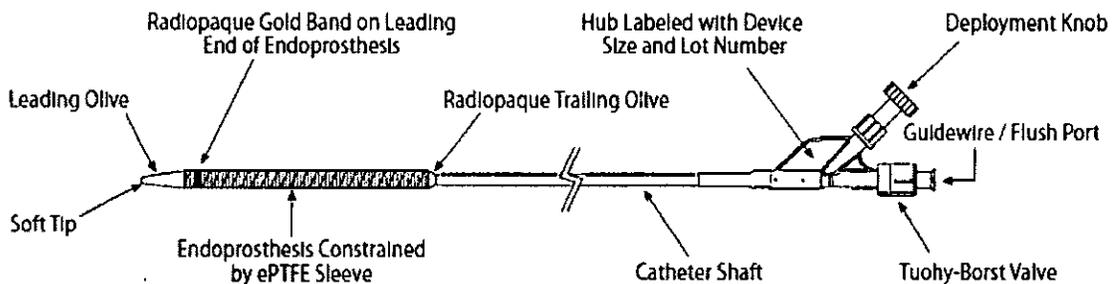


Figure 1. Conformable GORE® TAG® Thoracic Endoprosthesis Delivery System

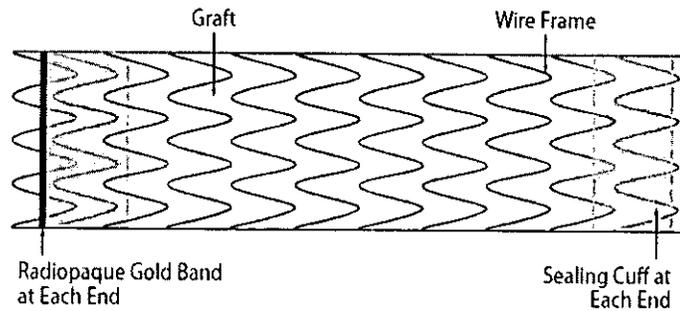


Figure 2. Conformable GORE® TAG® Thoracic Endoprosthesis

Table 1. Conformable GORE® TAG® Thoracic Endoprosthesis Sizing Guide

Endoprosthesis Diameter (mm)	Intended Aortic Diameter (mm)	Endoprosthesis Length (cm)	Recommended Sheath Size (Fr)	Part Numbers
21	16-19.5	10	18	TGU212110
26	19.5-24	10	20	TGU262610
28	22-26	10, 15	20	TGU282810, TGU282815
31	24-29	10, 15	22	TGU313110, TGU313115
34	27-32	10, 15, 20	22	TGU343410, TGU343415, TGU343420
37	29-34	10, 15, 20	24	TGU373710, TGU373715, TGU373720
40	31-37	10, 15, 20	24	TGU404010, TGU404015, TGU404020
45	34-42	10, 15, 20	24	TGU454510, TGU454515, TGU454520
26 (proximal) 21 (distal)	19.5-24 (proximal) 16-19.5 (distal)	10	20	TGU262110
31 (proximal) 26 (distal)	24-29 (proximal) 19.5-24 (distal)	10	22	TGU312610

VI. Alternative Practices and Procedures

Alternative treatment of isolated lesions of the descending thoracic aorta (DTA) depends upon the specific etiology being treated.

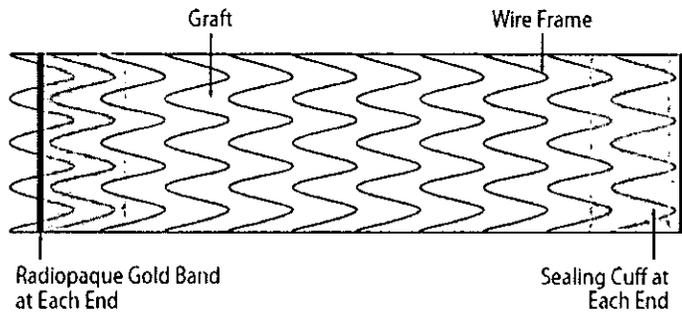


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31	24-29	10, 15	22	TGU313110, TGU313115
34	27-32	10, 15, 20	22	TGU343410, TGU343415, TGU343420
37	29-34	10, 15, 20	24	TGU373710, TGU373715, TGU373720
40	31-37	10, 15, 20	24	TGU404010, TGU404015, TGU404020
45	34-42	10, 15, 20	24	TGU454510, TGU454515, TGU454520
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VI. Alternative Practices and Procedures

Alternative treatment of isolated lesions of the descending thoracic aorta (DTA) depends upon the specific etiology being treated.

For non-emergent etiologies, such as stable lesions of the DTA, regular observation and medical management is the first choice for treatment. Medical management usually includes reducing blood pressure, reducing cholesterol, and minimizing other risk factors through the administration of drugs and lifestyle adaptations. However, surgical or endovascular intervention may be recommended if factors such as lesion diameter, rate of growth, and/or the presence of symptoms indicate an increased risk of aortic rupture. For emergent etiologies, such as transections, surgical or endovascular intervention is required to prevent death.

VII. Marketing History

The GORE® TAG® Thoracic Endoprosthesis originally received premarket approval for use in the treatment of aneurysms of the DTA on March 23, 2005 (P040043). The design changes that resulted in the conformable GORE® TAG® Thoracic Endoprosthesis received premarket approval for use in the treatment of aneurysms of the DTA on August 23, 2011 (P040043/S039).

Previous changes to the device include modifications to the device's delivery catheter (P040043/S024, approved November 7, 2008) and the addition of a 45mm diameter variant of the device (P040043/S031, approved March 23, 2010).

Outside the United States, the device has been marketed for nearly fourteen years for use in the endovascular repair of the descending thoracic aorta. The CTAG Device design iteration has been commercially distributed outside the US since 2009.

VIII. Potential Adverse Effects of the Device on Health

Adverse effects or 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 (to contrast, anti-platelet therapy, stent graft material)
- Amputation
- Anesthetic complications
- Aneurysm rupture
- Angina
- Atelectasis / pneumonia
- Bleeding (procedural and post-treatment)
- Bowel (e.g., ileus, transient ischemia, infarction, necrosis)
- Branch vessel occlusion
- Cardiac (e.g., arrhythmia, myocardial infarction, congestive heart failure,
- Excessive or inappropriate radiation exposure
- Femoral neuropathy
- Fever and localized inflammation
- Fistula (aortoenteric, arteriovenous, aorto-esophageal, aortobronchial)
- Genitourinary (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- Hematoma
- 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 ischemia
- Post-implant syndrome

- 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
- 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.

X. Summary of Primary Clinical Studies

One primary clinical study and one additional study were conducted to support the expanded indication of isolated lesions of the DTA for the CTAG Device. Key characteristics of the clinical studies are provided in **Table 6** below.

It should be noted that the safety of the CTAG Device for isolated lesions of the DTA was not based on the TAG 08-02 (transection) and TAG 04-01 (ruptured aneurysm) 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) that was reviewed under another PMA Supplement (P040043/S039) for the CTAG Device. Further discussion of the supplementary information considered along with relevant factors regarding the patient populations covered under the indication of isolated lesions of the DTA will be provided subsequently along with clinical background information on key pathologies which comprise isolated aortic lesions.

Table 6. Primary Clinical Studies

Clinical Study	Study Design	Objective	Number of Sites	Number of Subjects
TAG 08-02 (Traumatic Aortic Transection Pivotal Study)	Prospective, non-randomized, multi-center, single arm	Describe the short term safety and effectiveness of the CTAG Device for treatment of subjects with traumatic aortic transection.	Maximum of 30 sites approved for participation A total of 21 sites enrolled subjects in the study cohort	51 enrolled subjects 51 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 (20 traumatic aortic transection subjects)

X.1. TAG 08-02 –Traumatic Aortic Transection Pivotal Study Design

The TAG 08-02 study (IDE G090008) was a prospective, non-randomized, multi-center, single arm evaluation of the CTAG Device in the treatment of traumatic transection of the DTA. The primary objective of this study was to describe the short term safety and effectiveness of the CTAG Device for treatment of subjects with traumatic aortic transection. The primary safety endpoint was all cause 30-day mortality. The primary effectiveness endpoint was the proportion of subjects free from an MDE through the 1 month post treatment window (0 to 59 days post treatment). An MDE was defined as any of the following events that require significant therapy, including unplanned increase in the level of care, permanent sequelae, hospitalization, or death:

- Endoleak
- Migration
- Wire fracture
- Compression
- Erosion
- Extrusion
- Aortic dilatation
- Endograft infection
- Aortic rupture

Although these endpoints were specified in the protocol, no formal hypothesis testing was planned for either of the endpoints. The sample size of 50 subjects was planned to provide a protocol specified level of precision around the estimated 30-day mortality.

This study design was considered appropriate because the effectiveness of the device for treatment of a transection would likely be no worse than that for an aneurysm, provided no unique device related issues were identified during the clinical study due to the different patient populations. With respect to safety, although use of the device is intended to avoid transection-related mortality, it is not possible to determine an appropriate performance goal as the deaths would likely be due to the associated injuries and not the treatment of the transection (i.e., the mortality rate would be based on the extent of patients' injuries and would not reflect the treatment) and, in fact, the expected number of deaths related to a failure of the device would be zero based on the aneurysm data. In summary, the current clinical study was intended to show that the treatment of transections with the CTAG Device did not introduce new concerns with safety and effectiveness.

There were three separate external evaluation groups that independently reviewed data for this study. They included a DSMB, a 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 08-02 study.

The CEC was utilized to review adverse event data to ensure consistent and accurate AE and death reporting and classification. The CEC reviewed and adjudicated the site reported device relationship to the AE as well as the AE severity for selected events (deaths, major adverse events, paraplegia, paraparesis, stroke and aortic rupture). Each event was independently reviewed by three CEC members.

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.

Enrollment Requirements

Subjects were screened and eligibility for enrollment into the study was determined by the Investigator. Pre-treatment evaluation included a contrast-enhanced spiral CTA of the chest, abdomen, and pelvis, with oblique, sagittal, and coronal reconstructions to assess aortic morphology and vascular characteristics. A physical exam was also conducted to assess medical history, subject risk status with Injury Severity Score and Glasgow Coma Scale Score, and inclusion/exclusion criteria, described below.

Inclusion criteria

- 1) Traumatic transection of the DTA that requires repair, determined by the treating physician
- 2) Traumatic aortic transection location between, but does not include, the left subclavian artery and celiac artery
- 3) Endovascular repair with the Conformable GORE® TAG® Device performed \leq 14 days after aortic injury
- 4) Age \geq 18 years
- 5) Proximal and distal landing zone length \geq 2.0 cm
 - a. Landing zones must be in native aorta
 - b. Landing zone may include left subclavian artery, if necessary
- 6) All proximal and distal landing zone inner diameters are between 16-42 mm

- a. Diameter assessed by flow lumen and thrombus, if present; calcium excluded
- 7) Subject capable of complying with study protocol requirements, including follow-up
- 8) Informed Consent Form signed by subject or legal representative.

Exclusion criteria

- 1) Differing proximal and distal neck diameters (aortic taper) outside the intended aortic diameter requirements (sizing guide) for a single endoprosthesis diameter and the inability to use devices of different diameters (in adherence to the sizing guide) to compensate for the taper
- 2) Tortuous or stenotic iliac and/or femoral arteries and inability to use a conduit for vascular access
- 3) Aneurysmal, dissected, heavily calcified, or heavily thrombosed landing zone(s)
- 4) Infected aorta
- 5) Subject has a systemic infection and may be at increased risk of endovascular graft infection
- 6) Planned coverage of left carotid or celiac arteries with the CTAG Device
- 7) Known degenerative connective tissue disease, e.g., Marfan or Ehler-Danlos Syndrome
- 8) Treatment in another drug or medical device study within 1 year of study enrollment
- 9) Known history of drug abuse
- 10) Pregnant female
- 11) Moribund patient not expected to live 24 hours with or without operation, determined by the treating physician
- 12) Injury Severity Score of 75
- 13) Subject has known sensitivities or allergies to the device materials.

In addition to pre-treatment evaluations, subjects enrolled in TAG 08-02 were required to comply with the schedule of events described in **Table 27**. This included returning for follow-up visits at 1 month, 6 months and annually thereafter through 5 years. Follow-up procedures required a physical examination, chest x-ray and a spiral CT scan of the chest at each follow-up visit

Table 27. TAG 08-02 Schedule of Assessments

Diagnostic Test	Pre-treatment	Treatment	Discharge	30 days	6 months	Annually for 5 years
Physical Examination	X		X	X	X	X
Spiral Computed Tomography	X		X	X	X	X

Angiography		X				
Chest X-ray			X	X	X	X

X.2. TAG 08-02 –Traumatic Aortic Transection Pivotal Study Accountability of PMA Cohort

Subjects were screened and enrolled per the protocol. Eighty-seven (87) patients were screened for eligibility in the TAG 08-02 study and 36 subjects were excluded from study participation (Figure 5). Reasons for exclusion from the study were anatomic (n=9), inability to obtain informed consent from the subject or their legally authorized representative (n=8), the inability of the subject to comply with protocol requirements (n=8, including history of drug abuse), ASA injury classification of V (n=4), greater than 14 days from time of injury to time of treatment (n=3), age less than 18 years (n=3), and unknown (n=1).

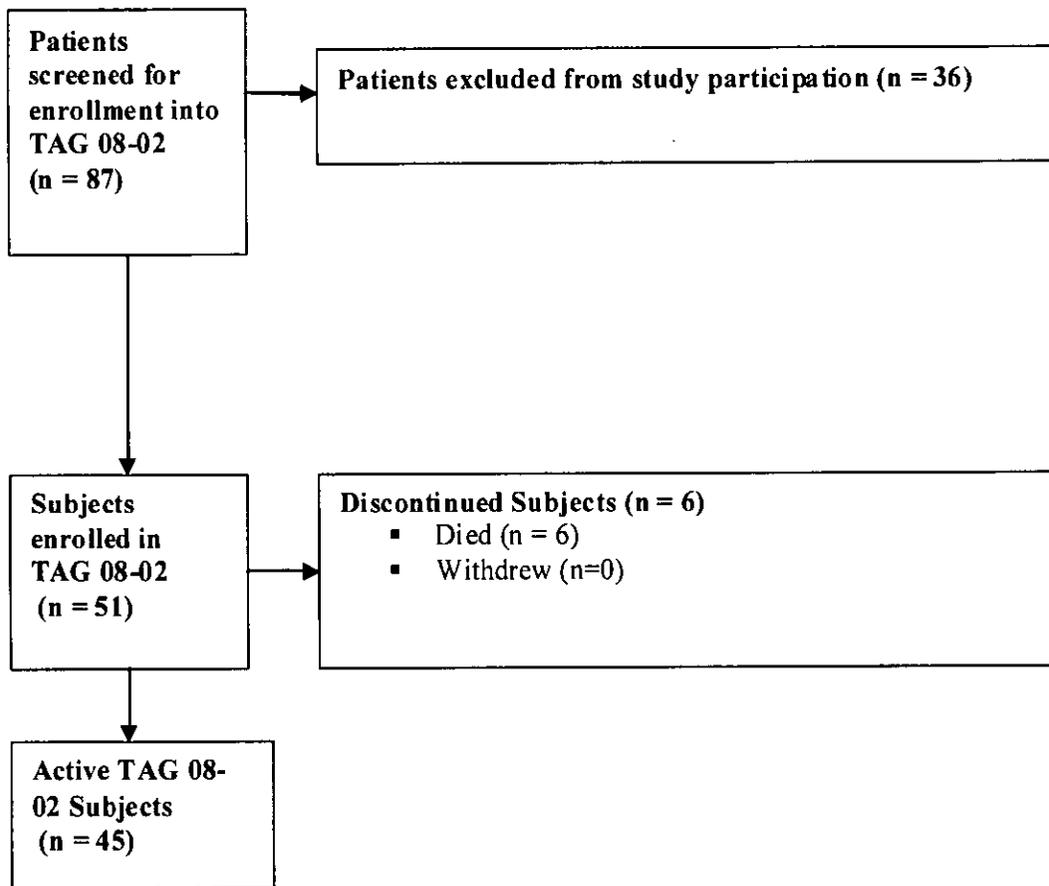


Figure 5. TAG 08-02 Enrollment Flowchart

A total of 51 subjects were enrolled at 21 investigative sites from December 2009 to January 2011. All enrolled subjects underwent endovascular repair with the CTAG Device to treat traumatic aortic transection.

Subjects enrolled in TAG 08-02 were required to return for follow-up visits as described in Table 27.

Table 28 summarizes compliance with protocol required visits and imaging along with discontinuation from the study. All subject visits through the 1 month interval are complete. Subjects remain in follow-up therefore data beyond 1 month are incomplete. Compliance with visit and imaging follow-up at 1 month is adequate to assess the study objectives.

Table 28. Subject Disposition and Compliance by Study Interval

Study Period	Eligible for follow-up ¹	Follow-up Compliance			Events Prior to Next Interval		
		Subjects with Visit in Window	CT Scan performed ^{1,2,3}	X-Ray performed ^{1,2,3}	Death ²	Discontinued ²	Not Due for Next F/U ²
Procedure	51	-	-	-	0 (0.0%)	0 (0.0%)	0 (0.0%)
Post-Procedure	51	-	-	-	3 (5.9%)	0 (0.0%)	0 (0.0%)
1 Month	48	47 (97.9%)	45 (93.8%)	43 (89.6%)	2 (4.2%)	0 (0.0%)	0 (0.0%)
6 Months	46	26 (56.5%)	23 (50.0%)	24 (52.2%)	1 (2.2%)	0 (0.0%)	23 (50.0%)
12 Months	22	7 (31.8%)	6 (27.3%)	6 (27.3%)	0 (0.0%)	0 (0.0%)	22 (100.0%)
24 Months	0	-	-	-	-	-	-
36 Months	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)

¹Subjects are considered eligible for follow-up if time on the study is on or after the first day of the given time window and they have not discontinued or died prior to the start of the interval.

²Percentages are based on number of subjects in visit window. Compliance is based on site reported imaging assessments.

³Refer to individual results tables for the number of subjects with adequate imaging to assess the parameters provided in that specific results table.

X.3. TAG 08-02 –Traumatic Aortic Transection Pivotal Study Population Demographics and Baseline Parameters

Baseline assessments of TAG 08-02 study subjects include demographics, injuries concomitant to the traumatic aortic transection, risk factor evaluations, medical history, presenting vital statistics, and radiological aortic assessment.

Table 29 provides a summary of demographic data. A majority of subjects (66.7%) were male. Caucasians comprised 82.4% of the cohort. Median subject age was 40 years (range: 21-87 years).

Subject medical history is presented in **Table 30**. Most commonly noted at the pre-treatment visit were history of smoking, hypertension, and hypercholesterolemia. In general, cardiac risk factors and comorbid conditions were uncommon in the TAG 08-02 cohort.

Table 31 summarizes pre-treatment risk using several criteria including American Society of Anesthesiology (ASA) risk classification, injury severity score (ISS), and Glasgow coma scale (GCS). Most subjects were classified as ASA IV, defined as severe systemic disease that is a constant threat to life. A large majority of subjects presented with polytrauma based on the ISS.

Table 32 summarizes commonly reported poly-traumatic injuries associated with the presenting traumatic injury. Most subjects (96%) presented with at least one concomitant injury in addition to the traumatic aortic transection. Commonly reported injuries included various fractures, chest and lung injuries and other damage to internal organs.

Pre treatment aortic measurements as reported by the investigational site are provided in **Table 33**. The median diameter at the proximal implantation site was 24mm. The median diameter at the distal implantation site was 21.9mm. The median lesion diameter was 28.6mm.

In summary, subjects presenting with traumatic aortic transections are relatively young and healthy compared to subjects with aneurysmal disease and they present to the hospital with polytrauma. Subjects treated for traumatic aortic transections tend to have smaller aortas, with localized injuries as compared to subjects with aneurysms. Although not specifically called out in the data below, these subjects also tend to have more angulated aortas as compared to the older subjects with aneurysmal disease.

Table 29. Subject Demographics

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Gender	
Male	34 (66.7%)
Female	17 (33.3%)
Ethnicity	
Not Hispanic or Latino	49 (96.1%)
Hispanic or Latino	2 (3.9%)
Race	
White or Caucasian	42 (82.4%)
Black or African American	5 (9.8%)
Asian / Oriental	2 (3.9%)
American Indian or Alaskan Native	1 (2.0%)
Native Hawaiian or Other Pacific Islander	1 (2.0%)
Middle Eastern	0 (0.0%)
Other	0 (0.0%)
Unknown	0 (0.0%)
Age (yrs)	
n	51
Mean (Std Dev)	44.1 (19.9)
Median	40.0
Range	(21.0, 87.0)
Weight (kg)	
n	51
Mean (Std Dev)	90.4 (20.0)
Median	85.4
Range	(63.0, 150.0)
Height (cm)	
n	51
Mean (Std Dev)	171.8 (10.7)
Median	171.5
Range	(152.4, 198.1)

Table 30. Subject Medical History

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Cigarette Smoking	15 (29.4%)
Hypertension	13 (25.5%)
Hypercholesterolemia	7 (13.7%)
CAD	4 (7.8%)
Diabetes Mellitus	4 (7.8%)
COPD	3 (5.9%)
CABG	2 (3.9%)
Renal Insufficiency	2 (3.9%)
CHF	1 (2.0%)
Carotid Disease	1 (2.0%)
Stroke	1 (2.0%)
TIA	1 (2.0%)
Peripheral Vascular Disease	0 (0.0%)

Table 31. Pre-Treatment Risk Summary

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
ASA Classification	
I	5 (9.8%)
II	5 (9.8%)
III	10 (19.6%)
IV	31 (60.8%)
V	0 (0.0%)
Injury Severity Score	
n	51
Mean (Std Dev)	31.8 (14.2)
Median	29.0
Range	(9.0, 66.0)
ISS Polytrauma	
Polytrauma (ISS>17)	43 (84.3%)
No Polytrauma (ISS<=17)	8 (15.7%)
Glasgow Coma Scale	
Minor >=13	41 (80.4%)
Moderate 9-12	5 (9.8%)
Severe <=8	4 (7.8%)
Missing	1 (2.0%)

Table 32. Presentation Injuries Reported in >5% of Study Subjects

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Any Concomitant Injury	50(98.0%)
Thoracic cage fractures and dislocations	41(80.4%)
Pneumothorax and pleural effusions NEC	33(64.7%)
Skin injuries NEC	30(58.8%)
Abdominal injuries NEC	24(47.1%)
Spinal fractures and dislocations	23(45.1%)
Upper limb fractures and dislocations	22(43.1%)
Chest and lung injuries NEC	20(39.2%)
Lower limb fractures and dislocations	16(31.4%)
Pelvic fractures and dislocations	16(31.4%)
Parenchymal lung disorders NEC	11(21.6%)
Skull fractures, facial bone fractures and dislocations	11(21.6%)
Non-site specific injuries NEC	8(15.7%)
Haemorrhages NEC	7(13.7%)
Mediastinal disorders	7(13.7%)
Site specific injuries NEC	7(13.7%)
Anaemias NEC	6(11.8%)
Limb injuries NEC (incl traumatic amputation)	6(11.8%)
Central nervous system haemorrhages and cerebrovascular accidents	5(9.8%)
Renal and urinary tract injuries NEC	5(9.8%)
Renal structural abnormalities and trauma	5(9.8%)
Urinary abnormalities	5(9.8%)
Vascular hypotensive disorders	5(9.8%)
Adrenal gland disorders NEC	4(7.8%)
Cerebral injuries NEC	4(7.8%)
Paralysis and paresis (excl cranial nerve)	4(7.8%)
Peritoneal and retroperitoneal haemorrhages	4(7.8%)
Renal vascular and ischaemic conditions	4(7.8%)
Respiratory failures (excl neonatal)	4(7.8%)
Skin and subcutaneous conditions NEC	4(7.8%)
Vascular hypertensive disorders NEC	4(7.8%)
Cardiovascular injuries	3(5.9%)
Pain and discomfort NEC	3(5.9%)
Rate and rhythm disorders NEC	3(5.9%)
Renal failure and impairment	3(5.9%)
Spinal cord and nerve root disorders NEC	3(5.9%)

Table 33. Pre-Treatment Aortic Measurements

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Aortic Diameter at Proximal Implantation Site (mm)	
n	51
Mean (Std Dev)	24.1 (3.7)
Median	24.0
Range	(17.0, 33.0)
Aortic Diameter 1cm from Proximal Implantation Site (mm)	
n	51
Mean (Std Dev)	23.4 (3.8)
Median	23.0
Range	(16.0, 35.0)
Aortic Diameter 2cm from Proximal Implantation Site (mm)	
n	51
Mean (Std Dev)	23.5 (3.7)
Median	23.0
Range	(16.0, 35.0)
Maximum Aneurysm/Lesion Diameter (mm)	
n	51
Mean (Std Dev)	29.2 (6.3)
Median	28.6
Range	(18.0, 47.0)
Aortic Diameter 2cm from Distal Implantation Site (mm)	
n	51
Mean (Std Dev)	21.9 (4.0)
Median	21.0
Range	(16.0, 32.0)
Aortic Diameter 1cm from Distal Implantation Site (mm)	
n	51
Mean (Std Dev)	21.8 (3.8)
Median	21.5
Range	(16.0, 32.0)
Aortic Diameter at Distal Implantation Site (mm)	
n	51
Mean (Std Dev)	21.8 (3.8)
Median	21.9
Range	(16.0, 34.0)
Proximal Neck Length (Aneurysm/Lesion-LCCA) (cm)	
n	51
Mean (Std Dev)	3.8 (3.4)
Median	3.0

Table 33. Pre-Treatment Aortic Measurements

	TAG 08-02 Cohort
Range	(2.0, 24.0)
Distal Neck Length (cm)	
n	51
Mean (Std Dev)	15.5 (5.8)
Median	17.0
Range	(2.0, 25.0)
Aneurysm/Lesion Length (cm)	
n	51
Mean (Std Dev)	2.8 (1.3)
Median	2.6
Range	(1.0, 7.7)
Left Common Iliac Diameter (mm)	
n	51
Mean (Std Dev)	10.0 (2.8)
Median	9.7
Range	(6.2, 25.0)
Left External Iliac Diameter (mm)	
n	51
Mean (Std Dev)	7.9 (1.5)
Median	8.0
Range	(4.8, 12.0)
Right Common Iliac Diameter (mm)	
n	51
Mean (Std Dev)	10.0 (2.1)
Median	10.0
Range	(6.5, 18.0)
Right External Iliac Diameter (mm)	
n	51
Mean (Std Dev)	8.0 (1.4)
Median	8.0
Range	(5.0, 11.0)

Treatment Details

Device use data are provided in **Table 34** and **Table 35**. The aortic lesion was excluded using only one device in 88% of the subjects, with a median of one device per case required. Only 3.5% of the devices implanted were 37mm or larger in diameter, with one subject requiring two 37mm devices. No 40mm or 45mm devices were used in the TAG 08-02 study. Conversely, smaller devices were frequently used, with 90% of the devices implanted being 31mm or smaller, including 28% using a 21mm device (either proximal or distal diameter) designed for aortic diameters from 16 – 19.5mm.

Most subjects required a single device which reflects the localized nature of their aortic lesions. This phenomenon is contrary to what is seen on thoracic aortic aneurysms where the aortic lesion is much longer and diffuse, and multiple devices are needed to accomplish a successful endovascular treatment. Also, most devices used were ≤ 28 mm maximum diameter which reflects that subjects presenting with traumatic aortic transections are younger and have non-dilated, non-aneurysmal aortas.

The TAG 08-02 procedural outcomes are displayed in **Table 36**. The LSA was completely or partially covered in 62.8% of study subjects with only 5.9% of study subjects receiving a bypass or transposition procedure.

A summary of convalescence is presented in **Table 37**. Median hospital stay after endovascular treatment with the CTAG Device was 13 days (range 2-73 days). All subjects had an intensive care unit (ICU) stay. The median length of ICU stay was 5.4 days. Hospital survival rate was 92.2%.

Table 34. Number of Endoprostheses Implanted

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Number of Subjects With Successful Initial Implant	51
Number of Implanted Endoprostheses (Initial Implant)	
1	45 (88.2%)
2	6 (11.8%)
n	51
Mean (Std Dev)	1.1 (0.3)
Median	1.0
Range	(1.0, 2.0)
Number of Subjects With Additional Implantation	0

Table 35. Implanted Device Characteristics

Proximal Diameter (mm)	Distal Diameter (mm)	Length (cm)	Initial Procedure	
			Subjects (N=51) n (%)	Devices (N=57) n (%)
21	21	10	5 (9.8%)	5 (8.8%)
26	21	10	10 (19.6%)	11 (19.3%)
26	26	10	11 (21.6%)	12 (21.1%)
28	28	10	8 (15.7%)	10 (17.5%)
31	26	10	8 (15.7%)	8 (14.0%)
31	31	10	4 (7.8%)	5 (8.8%)
34	34	10	4 (7.8%)	4 (7.0%)
37	37	10	1 (2.0%)	2 (3.5%)

Table 36. Summary of Procedural Outcomes

	TAG 08-02 Cohort
Number of Enrolled Subjects¹	51
LSA Procedure	
None	48(94.1%)
Transposed	1(2.0%)
Bypassed	2(3.9%)
Access Site	
Femoral Artery	49(96.1%)
Iliac Artery	1(2.0%)
Infrarenal Aorta	1(2.0%)
Anesthesia Method	
General	47(92.2%)
Regional	1(2.0%)
Local	3(5.9%)
Adjunctive Techniques to Prevent Paraplegia¹	
CSF Drainage	1(25.0%)
Induced Hypertension	2(50.0%)
Other	1(25.0%)
Proximal Implantation Zone	
Zone 2	32(62.7%)
Zone 3 / Zone 4	19(37.3%)
LSA Coverage	
Complete	17(33.3%)
Partial	15(29.4%)
None	19(37.3%)

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

Table 37. Summary of Subject Convalescence

	TAG 08-02 Cohort	95%.CI
Number of Enrolled Subjects	51	
Hospitalization Duration (Days)		
n	51	
Mean (Std Dev)	14.6 (12.3)	(11.2, 18.0)
Median	13.0	
Range	(2.0, 73.0)	
ICU Stay		
Yes	51 (100.0%)	(93.0%, 100.0%)
No	0 (0.0%)	
ICU Days		
n	51	
Mean (Std Dev)	8.2 (7.9)	(6.1, 10.4)
Median	5.4	
Range	(0.7, 36.5)	
Intubation		
Yes	40 (78.4%)	
No	11 (21.6%)	
Ventilator Days		
n	50	
Mean (Std Dev)	6.5 (11.8)	
Median	1.0	
Range	(0.0, 60.0)	
Hospital Survival	47 (92.2%)	

X.4. TAG 08-02 –Traumatic Aortic Transection Pivotal Study Safety and Effectiveness Results

Safety Evaluation

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 consists of all enrolled subjects.

Results for the primary endpoint are displayed in **Table 38**. A total of 4 subjects died within 30 days post-procedure. This result demonstrates a 30 day mortality rate of 7.8% for traumatic aortic transection subjects treated with the CTAG Device.

Table 38. Primary Safety Endpoint

Enrolled	Eligible for Primary Endpoint Analysis	Number of 30-Day Deaths	30-Day Mortality Percentage (95% CI)
51	51	4	7.8% (3.1%, 18.5%)

Subject Deaths

A total of six TAG 08-02 study subjects have died throughout the course of the study. All deaths were determined by the CEC to be unrelated to the device or procedure. A listing of all deaths is provided in **Table 39**.

Table 39. Subject Deaths

Subject Number	Procedure Date	Death Date	Study Day	Cause of Death	Related to Device or Procedure ¹
0802-116-005	08JAN2011	10JAN2011	2	Cardio-respiratory arrest	Unrelated to device or endovascular procedure
0802-158-005	20OCT2010	06NOV2010	17	Shock	Unrelated to device or endovascular procedure
0802-179-001	07JUN2010	28DEC2010	204	Drug toxicity	Unrelated to device or endovascular procedure
0802-179-004	10NOV2010	22NOV2010	12	Respiratory failure	Unrelated to device or endovascular procedure
0802-424-003	21MAY2010	17JUL2010	57	Traumatic brain injury	Unrelated to device or endovascular procedure
0802-429-009	08OCT2010	09OCT2010	1	Splenic haemorrhage	Unrelated to device or endovascular procedure

¹As adjudicated by the CEC.

Serious Adverse Events

Serious adverse events (SAE) reported in the first 30 days post-procedure are summarized in **Table 40**. Of the subjects that reported an SAE within 30 days post-procedure, 20 (39.2%) subjects had at least one SAE reported, and 10 of those subjects had more than one SAE reported.

Although it is important to report all SAEs observed within the first 30 days following the procedure, in the setting of traumatic transection and concomitant polytrauma it is also reasonable to assess the relationship of these events to the device and endovascular procedure. The CEC adjudicated all of the events in **Table 40** as unrelated to the endovascular procedure or the device with the exception of one ischaemic stroke.

Table 40. Summary of Serious Adverse Events through 30 Days

	TAG 08-02 Cohort
Number of Enrolled Subjects	51
Any Serious Event	20(39.2%)
Pleural effusion	3(5.9%)
Respiratory failure	3(5.9%)
Anuria	2(3.9%)
Hypotension	2(3.9%)
Hypoxia	2(3.9%)
Ileus	2(3.9%)
Pneumonia	2(3.9%)
Pyrexia	2(3.9%)
Abnormal weight gain	1(2.0%)
Acute respiratory distress syndrome	1(2.0%)
Acute respiratory failure	1(2.0%)
Anaemia	1(2.0%)
Angina pectoris	1(2.0%)
Atrial fibrillation	1(2.0%)
Blood culture positive	1(2.0%)
Cardio-respiratory arrest	1(2.0%)
Cerebral hypoperfusion	1(2.0%)
Dyspnoea	1(2.0%)
Enterococcal infection	1(2.0%)
Fat embolism	1(2.0%)
Haematemesis	1(2.0%)
Haematocrit decreased	1(2.0%)
Haemodynamic instability	1(2.0%)
Heart rate increased	1(2.0%)
Hypertension	1(2.0%)
Hypoxic-ischaemic encephalopathy	1(2.0%)
Ischaemic stroke	1(2.0%)
Joint contracture	1(2.0%)
Leukocytosis	1(2.0%)
Non-cardiac chest pain	1(2.0%)
Pneumothorax	1(2.0%)
Postoperative wound infection	1(2.0%)
Renal failure	1(2.0%)
Respiratory tract infection	1(2.0%)
Septic shock	1(2.0%)
Shock	1(2.0%)
Skin infection	1(2.0%)
Splenic haemorrhage	1(2.0%)
Splenic injury	1(2.0%)
Supraventricular tachycardia	1(2.0%)
Tachycardia	1(2.0%)
Traumatic brain injury	1(2.0%)
Traumatic liver injury	1(2.0%)
Wound infection staphylococcal	1(2.0%)

Effectiveness Evaluation

Gore collected adverse device event data to evaluate the effectiveness of the CTAG Device. Device effectiveness was assessed in two ways.

First, 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 08-02 protocol. The site reported data were used for the effectiveness endpoint analysis.

Second, 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. Core lab data was not used for the primary endpoint analysis because the core lab was not able to classify device events as major per the protocol definition as they did not have access to subject medical information.

Primary Effectiveness Endpoint Analysis

The primary effectiveness endpoint for this study was a composite of MDEs requiring reintervention through 1 month of follow-up.

All enrolled subjects are included in the primary effectiveness endpoint analysis population. For effectiveness assessments requiring imaging, a window of up to 59 days for the one month assessment was allowed in the study protocol. Therefore, the endpoint was computed using Kaplan-Meier methods as follows:

- Subjects who experienced an MDE on or before post-operative day (POD) 59 were considered events in the analysis, with the event time set as the onset of the first such event.
- Subjects who completed at least 59 days of follow-up without experiencing an MDE on or before POD 59 were censored at 59 days.
- Subjects who completed less than 59 days of follow-up without experiencing an MDE were censored at the time of last contact.

No subjects experienced an MDE through 1 month post-procedure, which results in 100% freedom from MDEs in the TAG 08-02 study cohort.

Device Events

No major device events were reported in the TAG 08-02 study. Two minor endoleaks were reported.

A minor Type II endoleak was reported POD 14 and required no treatment.

A minor Type III endoleak (fabric tear) was reported at time of treatment and continuing through discharge. This event was reviewed by three members of the CEC. Specifically, they reviewed the following images:

- pre-deployment angiograms
- procedural angiograms post-deployment of first CTAG Device
- procedural angiograms post-deployment of second CTAG Device
- discharge CTA
- 30 day follow-up CTA

The CEC members were asked to determine whether or not an endoleak was present within each imaging time point listed above and if so what type of endoleak was present. To be consistent with the CEC review process for this study, the majority determination was considered the final CEC decision for this event. Two out of the three members determined that the endoleak had resolved by the end of the procedure (after deployment

of the second device), therefore, the final CEC decision is that there was no endoleak at the end of the procedure even though the site reported an ongoing endoleak at discharge. The CEC review for this study is considered an independent review and as such, may differ from site reported data as it does in this case.

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)
- device related issues (post-implant only).

There were no endoleaks, ruptures, fractures, extrusions/erosions, lumen obstructions, device compressions or thrombi in core lab data. The core lab detected one prosthesis migration of >10mm. No clinical sequelae were noted in relation to the device migration. This event did not count as an MDE for the primary endpoint analysis because the core lab did not perform the required clinical assessment of the subject along with the imaging review. Therefore, the event could not be classified as major or minor by the core lab and could not be included in the primary endpoint analysis.

Subgroup Analysis (Gender)

The TAG 08-02 study accrued a total of 17 (33%) female and 34 (67%) male subjects. Information on the gender distribution of traumatic aortic transection in the general population was estimated based on a publication by Demetriades et al. in the Journal of Trauma.¹ The authors presented the demographics for a multicenter series of patients treated with open and endovascular repair of traumatic aortic transection from a clinical trial. The percentage of females in this article was 24% of the total, 19% for open repair and 27% for endovascular repair. The distribution in the TAG 08-02 study is similar.

A post hoc analysis of death and SAEs by gender was performed. These results are presented in **Table 41** and **Table 42**. Sufficient patient numbers are not available to determine whether there is a difference in outcomes between male and female subjects.

Table 41. TAG 08-02 Overall Mortality by Gender

	All	Females	Males
Number of Enrolled Subjects	51	17	34
Any Mortality			
Yes	6(11.8%)	3(17.6%)	3(8.8%)
No	45(88.2%)	14(82.4%)	31(91.2%)

¹ Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. J Trauma 2008;64:561-570; discussion 570-561

Table 42. TAG 08-02 30-Day SAEs by Gender

	All	Females	Males
Number of Enrolled Subjects	51	17	34
Any 30-Day Serious Adverse Event			
Yes	20(39.2%)	11(64.7%)	9(26.5%)
No	31(60.8%)	6(35.3%)	25(73.5%)

X.5. TAG 04-01 – DTA Complex Aortic Pathologies Feasibility Study Design and Result Summary

The TAG 04-01 study (IDE G970267/S101) was a multi-center study originally planned to assess the initial feasibility of stent graft treatments for complex aortic pathologies of the DTA, including traumatic aortic transection. A total of 14 sites participated in the study enrolling 59 total subjects. Specifically, 11 of the 14 sites enrolled a total of 20 traumatic transection subjects. Currently available long term data from the traumatic aortic transection cohort of subjects enrolled in the study support the feasibility of the use of the TAG Device in this pathology.

Short term results from the TAG 04-01 traumatic aortic transection cohort are consistent with contemporary results from meta-analyses and other investigations into the treatment of traumatic aortic transection using thoracic stent grafts. In the TAG 04 01 traumatic aortic transection cohort, 30 day mortality was 5.0% (1/20 subjects). One event of spinal cord ischemia (SCI) resulting in complete paraplegia was also reported (5.0%). Recent clinical practice guidelines for the management of traumatic thoracic injury published by the Society for Vascular Surgery (SVS) reported a systematic review of published literature which included 9.0% mortality and 3.0% SCI.² A similar meta-analysis by Tang et al.³ reported 0.0% paraplegia and 7.6% mortality. Another prospective non randomized study which enrolled 125 subjects treated with stent-grafts for traumatic aortic transection⁴ reported 7.2% mortality and one paraplegia (<1.0%). Operative and short term clinical results from the TAG 04-01 traumatic aortic transection cohort are similar to published results on the treatment of traumatic aortic transection.

Device compression was identified as a failure mode of the TAG Device during the conduct of the TAG 04-01 study through post-market surveillance reports and TAG 04-01 study data. Three cases of device compression were observed in the TAG 04-01 traumatic aortic transection cohort. All three device compressions observed had a risk factor for the event; one was noted in a subject with landing zone diameters less than the required minimum, 23 mm; the other two events were observed in devices that were deployed with no proximal apposition to the inner curve of the aorta. When the TAG Device was used within the 23-37 mm aortic diameter range as required per protocol and deployed with adequate proximal seal, no device compressions were observed. In each circumstance within the study, the compression events were able to be resolved with additional procedures (additional TAG Device placement, bare metal stent placement, conversion to open repair). Notably, all major device events reported in the TAG 04-01 traumatic aortic transection cohort were associated with these three cases. These included the compression events themselves and concomitant Type IA endoleaks in two of the compression cases. Extended four year follow-up data collected on the subjects in the traumatic aortic transection cohort have identified only one other device event; a minor Type IA endoleak noted at the initial procedure that resolved without treatment.

² Murad MH, Rizvi AZ, Malgor R, et al. Comparative effectiveness of the treatments for thoracic aortic transection. *J Vasc Surg* 2011;53:193-199.e1-21

³ Tang GL, Tehrani HY, Usman A, et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. *J Vasc Surg* 2008;47:671-675

⁴ Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. *J Trauma* 2008;64:561-570; discussion 570-561

Long term follow-up data following the initial 30 day post-procedure data from the TAG 04-01 traumatic aortic transection cohort have identified no unexpected adverse events. Following the 6 month interval, few additional major adverse events have been reported. Many of the reported major adverse events at the later time intervals are in subjects who never recovered functionally from the initial traumatic injury. No device events were reported during any follow-up intervals after 6 months.

In summary, data collected in the TAG 04-01 traumatic aortic transection cohort have provided reasonable evidence that the TAG Device is a feasible treatment option in the treatment of traumatic aortic transection. Short term mortality and paraplegia outcomes are reflective of published studies and case series of the treatment of traumatic aortic transection using endovascular stent grafts. Aside from device compression and complications associated with compression (a recognized failure mode of the TAG Device when used outside of recommended sizing guidelines), no major device events were reported either during early or late follow-up. No unanticipated adverse events were observed through 4 years of follow-up.

XI. Supplementary Clinical Data on Traumatic Aortic Transection

The following supplementary information was provided in the PMA submission:

- 14 TAG 08-02 subjects enrolled under continued access for IDE G090008;
- 11 Emergency Use patients treated for traumatic transaction under IDE G090008 and IDE G090010;
- A review of product complaint data related to device compression with the TAG and CTAG Devices; and
- A review of selected peer reviewed literature.

XI.1. TAG 08-02 Continued Access Subjects

Fourteen (14) subjects were enrolled under the continued access (CA) protocol amendment, 12 of which had available data at time of database lock. These subjects were enrolled under identical inclusion/exclusion criteria as the study subjects and are subject to the same study follow-up requirements as the first 51 subjects enrolled. However, data entry and review was on-going for these subjects at the time of PMA submission so there is limited information available for all subjects. All subjects survived the treatment procedure and there was one minor type II endoleak reported for 1 subject, which required no reintervention.

XI.2. CTAG Device Emergency Use Patients

Emergency Use patients are patients that do not meet the inclusion/exclusion criteria for the study yet require emergent treatment of their injuries or condition and have no alternative treatment other than the investigational device. These patients are treated outside the study per the physician's standard of care and are not subject to the follow-up requirements of the study protocol. Below is the information known for these patients.

- All 11 patients survived the treatment procedure.
- Nine (9) patients were discharged from the hospital.
- Two (2) patients died within 30 days of treatment due to their traumatic injuries.
- One adverse event was reported involving an emergency use patient. This event was a catheter breakage during removal through an 18 Fr Cook Check-Flo Valve Sheath. No harm was reported to the patient at the time of the procedure and no additional events have been reported post-operatively. The CTAG Device labeling has been updated to warn against compatibility issues with sheaths of this type.

XI.3. Device Compression Product Complaint / OUS Data Review

Following commercialization of the TAG Device, the Sponsor established a post-market surveillance system which is designed to collect product complaints. Analysis of the post-market surveillance data for the TAG Device shows that 50.3% of the reported device compressions were in patients treated for traumatic aortic transection. **Table 43** displays the distribution of compression complaints by pathology treated. Figure 6 further describes the timing of TAG Device compression complaints in relation to date of

implant for traumatic aortic transection cases. The majority of compression complaints occurring in traumatic aortic transection patients (81.1%) occurred within 59 days (within the 1 month post-implantation window for the TAG 08-02 study).

Table 43. Summary of TAG Device Compression Complaints

	Number (%)
Total Number of Compression Complaints	181
Aneurysm	22(12.2%)
Dissection	44(24.3%)
Traumatic Aortic Transection	91(50.3%)
Other/Unknown	24(13.3%)

All data received through Sponsor's post-market surveillance system.

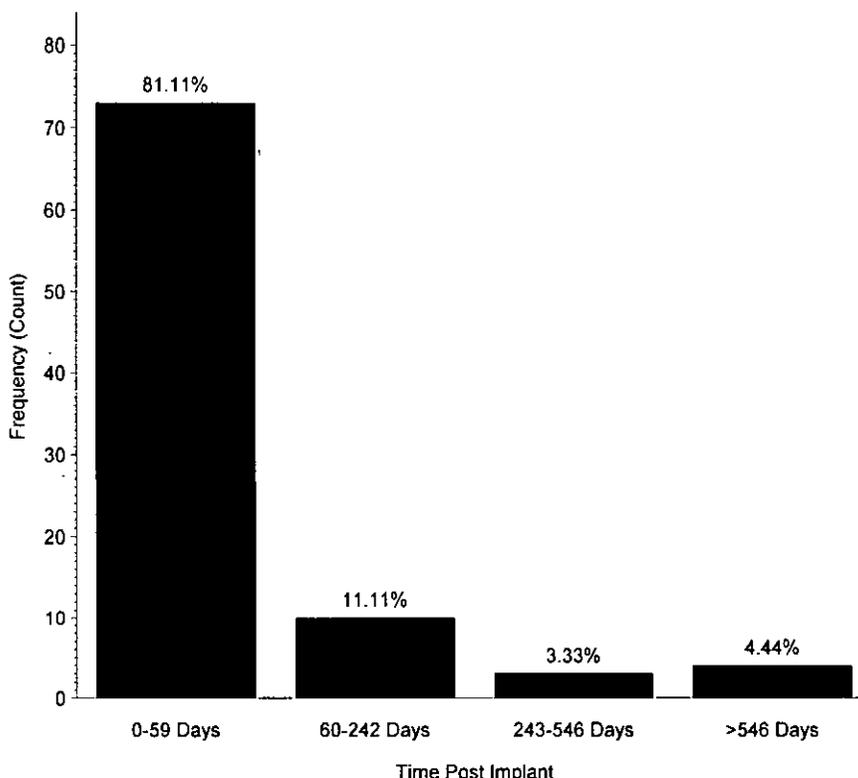


Figure 6. Timing of TAG Device Compression Complaints in Traumatic Aortic Transection

The CTAG Device, the subject of this PMA submission, is a modification of the TAG Device. Reducing the risk of device compression was one reason for the device modifications. The CTAG Device has been commercialized in Europe as well as other markets worldwide since October 2009 and post-market surveillance data have been collected since that time. The CTAG Device is approved for general endovascular repair of the DTA in Europe and other markets. There have been over 2200 commercial CTAG Devices sold through April 2011 and no device compressions have been reported.

XI.4. Literature Review

The treatment options for traumatic aortic transection include non-operative management, open surgical repair, and thoracic endovascular aortic repair (TEVAR), which excludes the lesion from circulation with an endovascular stent graft. The choice of therapy for traumatic aortic transection is patient dependent, and includes consideration of anatomy, concomitant injuries and suitability for surgery.

Relevant peer reviewed literature containing treatment outcomes for traumatic aortic transection was reviewed. Articles were selected based on their reporting of mortality for TEVAR and open surgical repair patients. One article also included outcomes from non-operative subjects. All but one paper reported mortality incidence and all compared mortality incidence between treatment modalities. Most of the reviewed articles (n=5) were meta-analyses using retrospective, non-randomized data while one article reported results for a prospective, non-randomized multi-center study. Reviewed articles included outcomes from between 193 and 7768 patients.

In TEVAR patients, reviewed literature reported mortality incidence ranging from 7.2% to 9.0% and one reported procedure related mortality of 2.0%. In all instances the TEVAR mortality was lower than open surgical repair, which ranged from 15.2% to 23.5%. The papers including incidence of paraplegia all showed lower rates in the TEVAR patients (0.0% to 3.0% versus 5.6% to 9.0% for open surgical repair). One article found the incidence of stroke to be significantly lower for TEVAR than for open surgical repair, although the other articles reporting stroke as an outcome did not show a significant difference. Summary data from recently published peer reviewed literature are displayed in **Table 44**.

Procedural outcomes for the CTAG Device study were favorable when compared with key results from peer reviewed literature.

Table 44. Literature Review

Article	Patient Group	Analysis Type	Outcomes Measured	Results**
Murad MH, Rizvi AZ, Malgor R, et al. Comparative effectiveness of the treatments for thoracic aortic transection. <i>J Vasc Surg</i> 2011;53:193-199.e1-21	139 studies with 7768 subjects (TEVAR, open, and non-operative)	Meta-analysis of literature	Mortality	9% TEVAR, 19% Open, 46% Non-operative; p<0.01
			Stroke	3% TEVAR, 3% Open, 2% Non-operative; p=0.9
			Spinal Cord Ischemia	3% TEVAR, 9% Open, 3% Non-operative; p<0.01
			End stage renal disease	3% TEVAR, 8% Open, 5% Non-operative; p<0.01
Xenos ES, Minion DJ, Davenport DL, et al. Endovascular versus open repair for descending thoracic aortic rupture: institutional experience and meta-analysis. <i>Eur J Cardiothorac Surg</i> 2009;35:282-286	22 retrospective cohort studies from 2003 to 2007. Includes 501 patients treated with open repair, 358 with TEVAR. Blunt thoracic aortic injury was pathology in 68% of patients	Meta-analysis of nonrandomized, retrospective studies	Mortality	OR=0.46 (0.26-0.78); p=0.005
			Paraplegia	OR=0.23 (0.08-0.065); p=0.005
Hoffer EK, Forauer AR, Silas AM, Gemery JM. Endovascular stent-graft or open surgical repair for blunt thoracic aortic trauma: systematic review. <i>J Vasc Interv Radiol</i> 2008;19:1153-1164	19 retrospective cohort studies. Outcomes of 262 TEVAR and 376 open repair subjects. Pooled analysis of 667 TEVAR survivors from 50 reports	Meta-analysis of nonrandomized, retrospective studies	Stroke	OR=0.86 (0.26-2.8); p=0.8
			Mortality	8.4% TEVAR, 20.2% Open, OR=0.43 (0.26-0.70); p=0.001
			Paraplegia	0.83% TEVAR, 5.7% Open, OR=0.30 (0.12-0.76); p=0.01
			Endoleak	Incidence 4.2%
Xenos ES, Abedi NN, Davenport DL, et al. Meta-analysis of endovascular vs open repair for traumatic descending thoracic aortic rupture. <i>J Vasc Surg</i> 2008;48:1343-1351	17 retrospective cohort studies with outcomes for 220 TEVAR and 389 open repairs	Meta-analysis of nonrandomized, retrospective studies	30 day mortality	8% TEVAR, 20% Open, OR=0.44 (0.25-0.78) p=0.005
			Procedure related mortality	2% TEVAR, 14% Open, OR=0.31 (0.15-0.66) p=0.002
			Post-operative paraplegia	0% TEVAR, 7% Open, OR=0.32 (0.1-0.93) p=0.037

Table 44. Literature Review

Article	Patient Group	Analysis Type	Outcomes Measured	Results**
Tang GL, Tehrani HY, Usman A, et al. Reduced mortality, paraplegia, and stroke with stent graft repair of blunt aortic transections: a modern meta-analysis. <i>J Vasc Surg</i> 2008;47:671-675	33 articles reporting 370 TEVAR and 329 open repair	Meta-analysis of nonrandomized, retrospective studies	Mortality Paraplegia Stroke	7.6% TEVAR, 15.2% Open; p=0.0076 0% TEVAR, 5.6% Open; p=0.0001 0.8% TEVAR, 5.3% Open; p=0.0028
Demetriades D, Velmahos GC, Scalea TM, et al. Operative repair or endovascular stent graft in blunt traumatic thoracic aortic injuries: results of an American Association for the Surgery of Trauma Multicenter Study. <i>J Trauma</i> 2008;64:561-570; discussion 570-561	TEVAR for 125 and open repair in 68 subjects	Prospective, nonrandomized multicenter studies	Mortality Procedure-related paraplegia Acute Respiratory Distress Syndrome ICU days mean \pm SD Hospital days mean \pm SD Blood transfusion (U) mean + SD	7.2% TEVAR, 23.5% Open; p=0.001 0.8% TEVAR, 2.9% Open; p=0.28 13.9% TEVAR, 18.2% Open; p=0.442 13.1 \pm 10.0 TEVAR, 14.00 \pm 15.1 Open; p=0.522 21.0 \pm 14.6 TEVAR, 27.3 \pm 50.3 Open; p=0.990 9.5 \pm 15.3 TEVAR, 12.0 \pm 19.1 Open; p=0.095

*Paper reported only event Odds Ratios (OR)

** All ORs displayed were calculated with event odds for open repair in denominator

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

In accordance with 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. Safety Conclusions

The adverse effects of the device are based on data collected in clinical studies conducted to support PMA approval as described above. Gore evaluated the safety of the CTAG Device through collection of site reported adverse events.

The primary safety endpoint for the clinical studies of the CTAG Device was all cause mortality incidence through 30 days post-treatment. No formal hypothesis testing was planned. The 30-day mortality rate for traumatic aortic transection subjects treated with the CTAG Device was 7.8%. This rate is comparable to that reported in the literature for treatment of traumatic aortic transection.

Of the subjects that reported an SAE within 30 days post-procedure, 20 (39.2%) subjects had at least one SAE reported, and 10 of those subjects had more than one SAE reported.

Although it is important to report all SAEs observed within the first 30 days following the procedure, in the setting of traumatic transection and concomitant polytrauma it is also reasonable to assess the relationship of these events to the device and endovascular procedure. The CEC adjudicated all of the SAEs as unrelated to the endovascular procedure or the device with the exception of one ischaemic stroke. The lack of device or endovascular procedure related events further supports the safety of this device.

The additional, supportive clinical information described above also supports the safety of the CTAG.

Information reviewed under a separate PMA supplement (P040043/S039) provided the additional information needed to support the safety of the broader indication of treatment of isolated lesions in the descending thoracic aorta. This additional information can be found in the Instructions for Use document.

B. Effectiveness Conclusions

Aneurysm and transection represent the two most common isolated lesion etiologies, all of which are treated in the same manner via exclusion from systemic pressure of the lesion with an endoprosthesis that achieves hemodynamic seal proximal and distal to the lesion.

The TAG Device was originally approved with an indication for treatment of aneurysms of the DTA. These patients are typically older (>70 years) and the disease process is the result of gradual expansion of the aorta over a period of years. These patients may also present with significant medical comorbidities, including hypertension, hypercholesterolemia, and other cardiac and non-cardiac related diseases.

The pre-specified primary effectiveness endpoint in the TAG 08-03 aneurysm study was met. This study demonstrated that the proportion of subjects (0.98) free from an MDE was greater than the pre-specified performance goal (0.83). No aneurysm ruptures, migrations, fractures, device compressions, or major endoleaks have been reported. To date, the most commonly reported device events have been minor endoleaks, which is consistent with historical TAG Device results. The TAG 08-03 study data collected to date demonstrate that the CTAG Device is effective in treatment of aneurysm of the DTA.

The TAG 08-03 results demonstrate representative aortic sizing for the degenerative aneurysm patient population, with median diameters of 29 and 30mm at the proximal and distal implantation sites, respectively. The median aneurysm diameter was 56mm. Multiple CTAG Devices were required to exclude the aneurysm in 53% of the cases, with a median of two devices implanted per case. Additionally, 54% of the implanted devices were 37, 40 or 45mm diameters which are intended to treat aortic diameters of 29-42mm. Although available during the conduct of the trial, no 21mm devices were used in the TAG 08-03 study.

The left subclavian artery (LSA) was involved in the treatment of the DTA aneurysm in 14 (27.5%) of the enrolled subjects in the TAG 08-03 study. In these non-emergent cases, LSA transposition or bypass was performed in 11/14 at or prior to the initial procedure.

The hospitalization details for the TAG 08-03 study included a median ICU stay of 2 days and total hospitalization duration for the index procedure of 4 days.

The traumatic transection patient population (in contrast to the degenerative aneurysm patient) is often characterized by younger patients with smaller aortic diameters which have generally healthy proximal and distal landing zones surrounding a focal aortic lesion. Complications in this patient population may not be related to the aortic lesion itself, which typically results from blunt force trauma to the chest that leads to shearing of the aorta, often near the aortic isthmus. Rather, these patients often have significant concomitant polytrauma (including closed head injuries, internal bleeding and organ damage) which can lead to immediate death independent of the aortic lesion. Notably, 98% of the TAG 08-02 subjects had at least one other concomitant injury at presentation.

The TAG 08-02 study subjects were younger than the TAG 08-03 subjects (median age 40 vs. 72 years) and had commensurately smaller aortic diameters (median of 24 and 22mm proximal and distal implantation site measurements). The aortic lesion was excluded using only one device in 88% of the subjects, with a median of one device per case required. Only 3.5% of the devices implanted were 37mm or larger in diameter, with one subject requiring two 37mm devices. No 40 or 45mm devices were used in the TAG 08-02 study. Conversely, smaller devices were frequently used, with 90% of the devices implanted being 31mm or smaller, including 28% using a 21mm device (either proximal or distal diameter) designed for aortic diameters from 16 – 19.5mm.

When compared with the TAG 08-03 study, the LSA was involved in the treatment of the TAG 08-02 subjects more frequently. A total of 32 subjects (63%) required device placement in Zone 2. The LSA was infrequently revascularized in these cases, with only 3 of the subjects undergoing bypass or transposition of the LSA. This suggests a different clinical approach to the management of the LSA in the emergent setting of traumatic aortic transection when compared with DTA aneurysms.

Hospitalization in the TAG 08-02 was prolonged relative to the TAG 08-03 study. Subjects required a median of 13 days in the hospital, and a median of 5.4 ICU days. In

general, the longer hospitalization and ICU stays for these subjects are due to concomitant polytraumatic injuries and not the aortic procedure itself.

TAG 04-01 results along with post-market surveillance identified device compression as a failure mode when used outside of the recommended sizing guidelines. No device compressions were identified in either CTAG Device study, and no device compressions have been reported through Gore's ongoing post-market surveillance of the CTAG Device outside the US.

C. 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.

Although there are differences between the traumatic transection and aneurysm patient populations, demonstrating the ability of the device to accommodate a wide range of aortic anatomies, there are also a number of similarities in the clinical treatment of these isolated lesions using an endovascular approach. Each pathology requires adequate proximal and distal aortic landing zone to achieve hemodynamic seal of the isolated lesion. Access and deployment techniques are the same. In general, the endovascular procedural steps and case planning are the same. The totality of evidence from the TAG 08-02 and TAG 08-03 studies, experience with the TAG Device commercially, and supplementary clinical information support labeling the CTAG Device with an indication for treatment of isolated lesions of the DTA.

Based on all data presented, the GORE® TAG® Thoracic Endoprosthesis has been demonstrated to be reasonably safe and effective in the endovascular repair of isolated lesions 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. Additionally, evaluation of the device in the treatment of dissections of the thoracic aorta has not been completed.

XIV. CDRH Decision

CDRH issued an approval order on January 13, 2012. The final conditions of approval cited in the approval order are described below.

You currently provide a clinical update to physician users at least annually with current information regarding your TAG device. Future clinical updates are to include information from your TAG 08-03 (aneurysm) and TAG 08-02 (transection) clinical studies. The information to be included for the TAG 08-03 study will be consistent with that reported for your other studies of treatment of aneurysms. At a minimum, the information to be included regarding TAG 08-02 will include a summary of the number of patients for whom data are available, with the rates of death, secondary endovascular procedures, conversion to open surgical repair, major device events, endoleak, prosthesis migration, losses of device integrity, aortic rupture and patency. Reports of losses of device integrity, reasons for secondary interventions and conversions to open surgical repair, and causes of death that may be associated with the lesion treated (e.g., death within 30 days of a secondary procedure to treat the index lesion and death from bleeding through the index lesion) are to be described. A summary of any

explant analysis findings are to be included. Additional relevant information from commercial experience within and outside of the US is also to be included. The clinical updates for physician users and the information supporting the updates must be provided in the Office of Device Evaluations (ODE) annual report.

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.