SUMMARY OF SAFETY AND EFFECTIVENESS DATA

General Information

Device Name

Generic Name: Endovascular Graft

Trade Name: GORE TAG Thoracic Endoprosthesis

Applicant's Name and Address

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Date of Panel Recommendation

January 13, 2005

Premarket Approval Application (PMA) Number

P040043

Date of Notice of Approval to Applicant

March 23, 2005

Indications and Usage

The GORE TAG Thoracic Endoprosthesis is intended for endovascular repair of aneurysms of the descending thoracic aorta (DTA) in patients who have appropriate anatomy including:

- Adequate iliac/femoral access
- Aortic inner diameter in the range of 23-37 mm
- ≥2 cm non-aneurysmal aorta proximal and distal to the aneurysm

Contraindications

There are no known contraindications for the GORE TAG Thoracic Endoprosthesis.

Warnings and Precautions

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

Device Description

The GORE TAG Thoracic Endoprosthesis provides a means for endovascular repair of the DTA. This device is a flexible, self-expanding endoprosthesis that is constrained on the leading end of a delivery catheter (**Fig. 1 and 2**). The system consists of two parts, the endoprosthesis and the delivery catheter. Endoprosthesis sizes range in diameter from 26mm to 40mm and in length from 10cm to 20cm (**Table 1**). The compressed profile of these devices on a delivery catheter ranges from 20-24Fr.

Endoprosthesis

The endoprosthesis consists of an expanded polytetrafluoroethylene (ePTFE) tube reinforced with ePTFE/FEP (fluorinated ethylene propylene) film and an external nitinol wire supporting structure that is attached circumferentially along the entire surface of the graft with ePTFE/FEP bonding tape. A circumferential PTFE sealing cuff is located on the external surface of the endoprosthesis at the base of each flared end. Each cuff is circumferentially attached on one edge with FEP allowing the other edge to remain free to enhance sealing of the endoprosthesis to the wall of the aorta. In order to facilitate accurate endoprosthesis placement, two radiopaque gold bands are attached to the graft at the base of each flared end.

A sleeve used to constrain the endoprosthesis on the leading end of the delivery catheter is made of ePTFE/FEP film. The sleeve is attached to the endoprosthesis with ePTFE fiber. The sleeve constrains the endoprosthesis and is sewn closed using an ePTFE deployment line, thereby constraining the endoprosthesis on the delivery catheter. The ePTFE sleeve remains in situ between the endoprosthesis and the vessel wall following deployment.

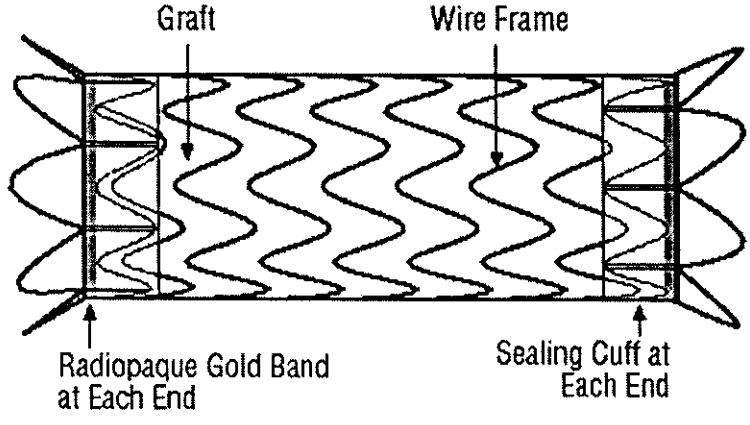

Figure 1. GORE TAG Thoracic Endoprosthesis

Delivery Catheter

The delivery catheter has a multi-lumen shaft reinforced with a stainless steel mandrel. One catheter lumen is for 0.035" guidewire access and a separate lumen contains the ePTFE deployment line. Two tapered oval beads or "olives" are located on the delivery catheter at each end of the endoprosthesis to provide a smooth transition from the delivery catheter to the constrained endoprosthesis.

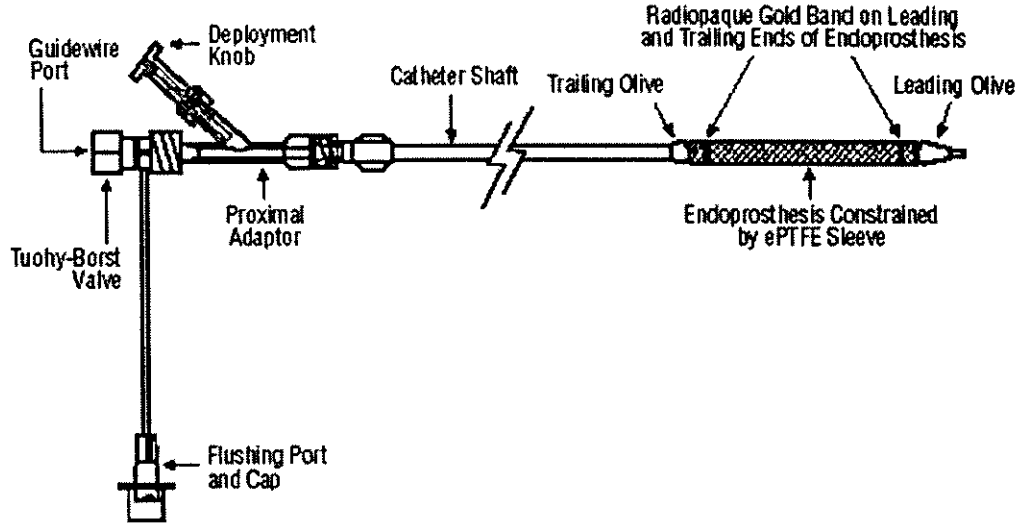

Figure 2. GORE TAG Thoracic Endoprosthesis Delivery Catheter

A two-arm adaptor is located on the proximal end of the delivery catheter. A Touhy-Borst valve is attached to the straight-arm and allows guidewire passage through the catheter. The Touhy-Borst valve also has a side flushing port that communicates with the guidewire lumen. A deployment knob is on the side-arm of the adaptor and attached to the deployment line. To release the endoprosthesis, the deployment knob is turned and pulled, which removes the deployment line from the constrained endoprosthesis with unlacing initiating in the middle of the endoprosthesis and simultaneously extending toward both ends. This allows the endoprosthesis to self-expand rapidly.

Table 1. GORE TAG Thoracic Endoprosthesis Sizing Guide

Intended Aortic Diameter (mm)	Endoprosthesis Diameter (mm)	Endoprosthesis Length (cm)	Recommended Sheath Size (Fr)	Part Numbers
23-24	26	10	20	TG2610
24-26	28	10, 15	20	TG2810, TG2815
26-29	31	10, 15	22	TG3110, TG3115
29-32	34	10, 15, 20	22	TG3410, TG3415, TG3420
32-34	37	10, 15, 20	24	TG3710, TG3715, TG3720
34-37	40	10, 15, 20	24	TG4010, TG4015, TG4020

Alternative Practices and Procedures

Medical management is the first choice for treatment, including reducing blood pressure and minimizing other risk factors. Medical management usually includes keeping your blood pressure under control, quitting smoking and reducing cholesterol in diet.

Open surgical repair is considered when the thoracic aortic aneurysm (TAA) is considered dangerous and at risk for rupture. The open procedure consists of a thoracotomy with surgical resection of the diseased aorta and replacement with prosthetic graft material. However, this procedure is associated with substantial mortality. Furthermore, operative morbidity incidence is considerable. Other common post-operative complications include paraplegia, bleeding, stroke, renal insufficiency, and need for prolonged ventilatory support.

However, both therapies have their limitations. Medical management does not treat the aneurysm, just reduces the stresses (i.e., blood flow pressure) on the aneurysm. Open surgical repair is invasive and not all patients can tolerate this major operation.

Marketing History

The original Gore TAG Thoracic Endoprosthesis received the CE mark in February 1998 and began distribution outside of the United States in December 1998. Gore discontinued distribution of the original TAG device in 2001 and began modifications to the design of the endoprosthesis.

The modified TAG device received the CE mark in February 2004 and began distribution in March 2004. The GORE TAG Thoracic Endoprosthesis is currently marketed in Asia, Australia, Europe, Latin America and New Zealand.

Adverse Events (TAG 99-01 & TAG 03-03)

Two U.S. clinical studies were conducted to evaluate the safety and effectiveness of the GORE TAG Thoracic Endoprosthesis. The first, referred to as TAG 99-01, evaluated the original design. The second U.S. clinical study, referred to as TAG 03-03, evaluated a modified version of the device. This Summary of Safety and Effectiveness contains the results of both of these U.S. clinical studies. The data from these studies were not pooled for the purpose of analysis. The first study demonstrated the one-year safety and effectiveness of the GORE TAG Thoracic Endoprosthesis. The second study demonstrated that the changes in the device did not adversely affect the clinical performance of the device. The study was focused on 30 day follow-up, as the device changes were only likely to affect deployment and also because the majority of device events in the first study occurred within the first 30 days.

Observed Adverse Events

For both clinical studies, 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

The first study (TAG 99-01) conducted at 17 investigational sites included 140 Test subjects (endovascular treatment) and 94 Control subjects (open surgical repair). The second study (TAG 03-03) conducted at 11 investigational sites included 51 Test subjects (endovascular treatment). The incidence of major adverse events (MAE) is reported in **Table 2**. Specific key major adverse events are delineated in **Table 3**.

Table 2. Major Adverse Events from US Clinical Studies

Safety endpoints	Post-treatment follow-up period (days)						
	0 - 30			31 - 365		366 - 730	
	TAG 99-01 (N = 140) n (%)	TAG 99-01 Control (N = 94) n (%)	TAG 03-03 (N = 51) n (%)	TAG 99-01 (N = 134) n (%)	TAG 99-01 Control (N = 85) n (%)	TAG 99-01 (N = 106) n (%)	TAG 99-01 Control (N = 66) n (%)
All-cause deaths	**2 (1)**	**6 (6)**	**0**	**22 (16)**	**14 (16)**	**10 (9)**	**4 (6)**
Aneurysm related deaths	2 (1)	6 (6)	0	2 (1)	3 (4)	0	0
Any major adverse event	**40 (29)**	**66 (70)**	**6 (12)**	**37 (28)**	**22 (26)**	**15 (14)**	**6 (9)**
Bleeding complications	13 (9)	50 (53)	0	3 (2)	1 (1)	2 (2)	0
Pulmonary complications	9 (6)	31 (33)	2 (4)	13 (10)	8 (9)	6 (6)	0
Cardiac complications	4 (3)	19 (20)	1 (2)	18 (13)	7 (8)	7 (7)	2 (3)
Renal function complications	2 (1)	12 (13)	0	4 (3)	3 (4)	1 (1)	0
Wound complications	8 (6)	11 (12)	1 (2)	1 (1)	3 (4)	1 (1)	1 (2)
Bowel complications	3 (2)	6 (6)	0	3 (2)	0	1 (1)	0
Vascular complications	20 (14)	4 (4)	3 (6)	5 (4)	2 (2)	0	0
Neurologic complications	11 (8)	30 (32)	1 (2)	4 (3)	4 (5)	3 (3)	1 (2)
Other major complications*	0	1 (1)	1 (1)	2 (1)	2 (2)	0	0
Reoperation	4 (3)	0	0	2 (1)	0	0	0
Rupture	0	0	0	0	0	0	0

Note: The difference between the TAG 99-01 and TAG 99-01 Control groups for any major adverse event at 1-year is statistically significant ($p<0.001$).

The difference between the TAG 03-03 and TAG 99-01 Control groups for any major adverse event at 30 days is statistically significant ($p<0.001$).

*aortoenteric fistula, prosthesis infection

Table 3. Key Major Adverse Events, TAG 99-01 (through 1 year)

Safety endpoints	TAG Device (N = 140) n (%)	Surgical Control (N = 94) n (%)
Bleeding complications		
Coagulopathy	1 (1)	9 (10)
Procedural	7 (5)	39 (41)
Post-procedural	4 (3)	13 (14)
Neurologic complications		
Cerebrovascular accident	7 (5)	7 (7)
Paraplegia / paraparesis / spinal neurological deficit	4 (3)	13 (14)
Pulmonary complications		
Respiratory failure	11 (8)	22 (23)
Renal function complication		
Renal failure	3 (2)	7 (7)
Vascular complications		
Vascular trauma	15 (11)	0

Potential Device or Procedure Related Adverse Events

Complications associated with the use of the GORE TAG Thoracic Endoprosthesis may include but are not limited to:

- adynamic ileus
- amputation
- angina
- aortoenteric fistula
- arteriovenous fistula
- atelectasis/pneumonia
- bleeding (procedural and post-treatment)
- bowel (e.g., ileus, transient ischemia infarction, necrosis)
- cardiac (e.g., arrhythmia, myocardial infarction, congestive heart failure, hypotension or hypertension)
- change in mental status
- coagulopathy
- death
- 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
- femoral neuropathy
- fever and localized inflammation
- genitourinary (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- hematoma
- infection (e.g., aneurysm, device or access sites)
- lymphocele/lymph fistula
- myocardial infarction
- neurologic damage, local or systemic (e.g., stroke, paraplegia, paraparesis)
- nerve injury
- 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)

Summary of Preclinical Results

Biocompatibility

Toxicology and biocompatibility testing was conducted for materials in the GORE TAG Thoracic Endoprosthesis. Testing was conducted in accordance with Federal Good Laboratory Practices per 21 CFR §58. The GORE TAG Thoracic Endoprosthesis was classified per ISO 10993 as an implant device with permanent contact. The GORE TAG Thoracic Endoprosthesis delivery catheter was classified as an externally communicating device with limited exposure (≤24 hr).

Table 4 summarizes the biocompatibility test results for the implant. **Table 5** summarizes the biocompatibility test results for the catheter.

Table 4. Biocompatibility testing of the TAG device

Test Name	Test Method	Results	Pass
Cytotoxicity	L929 MEM Elution Test – USP	Non-toxic	√
	Agarose Overlay-USP	Non-toxic	√
Pyrogenicity	LAL Testing, Kinetic Turbidimetric Method- USP	Non-pyrogenic	√
	Rabbit Pyrogen Test (Material Mediated) – ISO	Non-pyrogenic	√
Genotoxicity/ Mutagenicity	*Salmonella typhimurium* and *Escherichia coli* Reverse Mutation Assay – ISO	Non-mutagenic	√
Sensitization	Kligman Maximization Test (Modified) – ISO	0% sensitization	√
Irritation/ Intracutaneous Reactivity	Intracutaneous Injection Test – ISO	Negligible irritant	√
Acute Systemic Toxicity	Systemic Injection Test – ISO	Negative	√
Hemocompatibility	Hemolysis – Rabbit Blood – ISO	Non-hemolytic	√
Chronic Toxicity	Ovine Implant Study	No systemic effects observed.	√
Subchronic Toxicity	Ovine Implant Study	No systemic effects observed.	√
Implantation	Ovine Implant Study	No systemic effects observed.	√

Table 5. Biocompatibility testing of the TAG delivery system

Test Name	Test Method	Results	Pass
Cytotoxicity	L929 MEM Elution Test – ISO	Non-cytotoxic	√
Pyrogenicity	Rabbit Pyrogen Test (Material Mediated) – ISO	Non-pyrogenic	√
Sensitization	Kligman Maximization Test (Modified) – ISO	0% sensitization	√
Irritation/ Intracutaneous Reactivity	Intracutaneous Injection Test – ISO	Negligible irritant	√
Acute Systemic Toxicity	Systemic Injection Test – ISO	Negative	√
Hemocompatibility	Hemolysis – Rabbit Blood – ISO	Non-hemolytic	√

All test results indicate that the materials and processes used to manufacture the TAG Thoracic Endoprosthesis implant and catheter are biocompatible and suitable for their intended use.

Product Testing

W. L. Gore & Associates, Inc. (GORE) conducted comprehensive pre-clinical bench and analytical testing on the final designs of the GORE TAG Thoracic Endoprosthesis (TAG) implant and delivery system. Results obtained from the in vitro test regimen provide evidence substantiating the safety and effectiveness of the GORE TAG Thoracic Endoprosthesis.

Delivery System Test Results Summary

Table 6 displays the results of in vitro tests performed on the TAG delivery system to access the implant location, accurately deploy the device, safely withdraw the delivery system catheter, maintain hemostasis, and be fluoroscopically visualized.

Table 6. Summary of TAG Delivery System Test Results

In Vitro Test	Relevant Functional Requirement	Summary of Acceptance criteria and Test Results
Delivery Catheter Leak Test	• Hemostasis of the delivery system	The leak resistance of the delivery catheter was evaluated. The data indicated there was 95% confidence that there is at least a 95% probability that any TAG delivery catheter will meet the minimum acceptance criteria of 45 psi. In addition, currently all catheters are 100% leak tested in manufacturing to ensure conformance to the established design specifications.
Delivery Catheter Tensile Bond Strength Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	The longitudinal tensile strength of the critical bonds and joints of the TAG delivery catheter were determined. There is a 95% confidence that there is at least a 95% probability that the minimum tensile strength of the delivery catheter will meet the acceptance criteria of 7lbs.
Delivery Catheter Torsional Bond Strength Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	This test was performed for characterization purposes. The torsional strength of the delivery catheter was characterized and was determined to have torsional bond strengths significantly in excess of clinical design requirements. Clinical evaluation indicates adequate torsional strength.
Delivery System and Endoprosthesis Radiopacity Confirmation Test	• Fluoroscopic visualization	The acceptance criteria of this test is that the TAG delivery system and endoprosthesis should be visible enough to permit safe and efficacious clinical use and have adequate visibility when compared to the appropriate reference items. The results of the *in vitro* radiopacity testing show that the radiopacity of the TAG delivery system and endoprosthesis demonstrated sufficient radiopacity for clinical use. Clinical evaluation indicates adequate radiopacity.
Deployment Line/Knob Assembly Tensile Strength Test	• Ability to deploy the implant	The tensile strength of the catheter deployment line/knob assembly was determined to demonstrate conformance to the acceptance criteria of greater than 5 lbs. There is a 95% confidence that there is at least a 99% probability that any individual deployment line/knob assembly tensile strength exceeds the maximum expected deployment force.
Endovascular System Deployment Force Test	• Ability to deploy the implant	The force required to deploy the TAG endoprosthesis was determined to meet the acceptance criteria of less than 5 lbs. There is a 95% confidence that there is at least a 99% probability that this force does not exceed the TAG delivery catheter deployment knob/line strength.
Endovascular System Deployment Reliability Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system	A comprehensive evaluation of *in vitro* deployment was conducted using anatomical models, including tortuosity and angulation. This comprehensive deployment reliability testing includes accessory compatibility, torque-ability, device expansion and delivery system withdrawal in various testing models. A 95% confidence of 98% probability of successful deployment was required to meet the acceptance criteria for this test. Binomial statistics demonstrate with a 95% confidence level that at least 98% of the TAG endovascular systems will deploy successfully when used in a manner consistent with labeling or under anticipated clinical use.

In Vitro Test	Relevant Functional Requirement	Summary of Acceptance criteria and Test Results
		The torque response of the delivery system and the torque effect on deployment reliability were also evaluated in this testing. All tested delivery systems exhibited acceptable torque response after being tracked through an *in vitro* aneurysmal deployment model. All tested delivery systems deployed successfully after being subjected to torque during deployment testing.
Endovascular System Non-Destructive Dimensional Testing	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system • Hemostasis of the delivery system	All TAG endovascular systems are currently 100% tested to ensure conformance to established design requirements, including 0.035 " guidewire compatibility, endovascular system profile (20, 22, 24 Fr), working length (100 cm), endoprosthesis compressed length (nominal 10, 15, 20 cm), and other visual requirements to ensure conformance to the established design specifications. Compatibility with recommended introducer sheath and guidewire has been demonstrated during clinical evaluations.
Endovascular System Simulated Use Test	• Ability to access the intended location • Ability to deploy the implant • Ability to withdraw the delivery system • Fixation effectiveness of the implant	Simulated use testing evaluated the accessory compatibility, deployment accuracy, device conformability and resistance to acute migration in a pulsatile straight and angulated aneurysmal model. Physiologic pulsatile pressure, flow, and temperature were used in the testing. Acceptance criteria include compatibility with the 0.035 " guidewire, and appropriate introducer sheath (20, 22, 24 Fr), accurate deployment to within ± 5 mm of the intended target and less than 5 mm of migration after withdraw of the delivery system. Results indicate acceptable accessory compatibility, deployment accuracy, device conformability and resistance to migration.
Sewn Sleeve Burst Strength Test	• Ability to access the intended location • Ability to deploy the implant	The burst strength of representative sewn sleeves were characterized (151 - 286 psi) and determined to be adequate to constrain the stent-graft prior to implantation and greater than the 75 psi acceptance criteria.

Implant Test Results Summary

Table 7 displays testing performed to assess deployment accuracy, fixation effectiveness, durability, ability to exclude the aneurysm (permeability considerations), modularity, sizing, patency, MRI compatibility, and ability to be fluoroscopically visualized. The modified device performed as well or better than the original device in all comparison testing.

Table 7. Summary of TAG Implant Test Results

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
Delivery System and Endoprosthesis Radiopacity Confirmation Test	• Fluoroscopic visualization	The acceptance criteria of this test is that the TAG delivery system and endoprosthesis should be visible enough to permit safe and efficacious clinical use and have adequate visibility when compared to the appropriate reference items. Expected tissue density was simulated through 30 mm thick aluminum block. The results of the *in vitro* radiopacity testing show that the radiopacity of the TAG delivery system and endoprosthesis demonstrated sufficient radiopacity for clinical use. Clinical evaluation indicates adequate radiopacity.
Endoprosthesis Bending Fatigue Test	• Durability and integrity of the implanted device	Bending fatigue testing evaluates the bending durability of the endoprosthesis in comparison to the appropriate control. Bending fatigue testing was developed specifically to accelerate the device to failure in order to evaluate the durability of the TAG device in an overlapped configuration and under extreme bending conditions (90° with 4 mm motion). The acceptance criterion for this test is that the modified device should demonstrate improved bending durability when compared to the original device. Results indicate improved bending durability and improved graft material durability of the modified TAG device when compared to the original device.
Endoprosthesis Bend Radius Test	• Ability to accurately deploy • Fixation effectiveness of the implant • Patency of the implant	This test is for characterization purposes only. The bend radii of the TAG device were characterized. The data indicate that the modified device is improved in bend radius over the original device. Clinical performance indicates that the TAG System is capable of accommodating the anatomy.
Endoprosthesis Burst Strength Test	• Durability and integrity of the implanted device	The burst strengths of the TAG components were determined for characterization. The burst strength of the device is not expected to be less than the graft material. All burst strengths exceeded this acceptance criterion.
Endoprosthesis Cyclic Corrosion Test	• Durability and integrity of the implanted device	This test is for characterization purposes only. The corrosion resistance of both the Nitinol wire and a finished stent-graft were analyzed using potentiodynamic polarization testing. Results indicate acceptable corrosion resistance. Clinical performance with the TAG Thoracic Endoprosthesis and the EXCLUDER Bifurcated Endoprosthesis indicate acceptable corrosion resistance in clinical use.
Endoprosthesis Dimensions Test	• Testing of the modularity of the endovascular system • Appropriate sizing of the implant	The outer diameters, wall thickness and length of the deployed TAG devices were determined. Acceptance criteria for these tests are specific to each device length (10, 15, 20 cm) and diameter (26, 28, 31, 34, 37, 40 mm) as listed in the appropriate product specifications. All devices tested met these specifications.
Endoprosthesis Finite Element Analysis	• Durability and integrity of the implanted device	This test determines appropriate stress/strain levels and does not have specific acceptance criteria. The location and magnitude of the maximum strains in the TAG Nitinol wire frame were analytically determined as a function of radial compression and expansion when subjected to manufacturing, catheter loading, deployment and an *in vivo* pulsatile loading environment. Peak strain magnitudes at simulated catheter loading are predicted to be below the ultimate tensile strain of the Nitinol wire. Maximum strain locations and values determined from the simulated *in vivo* pulsatile loading were subsequently used as a reference in appropriate *in vitro* testing including pulsatile fatigue testing.
Endoprosthesis *In Vitro* Ultrafiltration Test	• Permeability considerations	To verify a decrease in transmural movement of serous fluid across the ePTFE graft wall, bench-top ultrafiltration testing was conducted. The acceptance criterion for this test is a reduction in leakage when compared to the original device. Results indicate that the modified TAG device demonstrates a reduction in transmural serous fluid movement across the ePTFE graft wall as compared to the original device when tested in this *in vitro* (bench-top) ultrafiltration model.
Endoprosthesis	• Durability and integrity	The longitudinal tensile strength of the TAG devices were determined for

In Vitro Test	Relevant Functional Requirement	Summary of Test Result
Longitudinal Tensile Strength Test	of the implanted device	characterization. The tensile strength of the device is not expected to be less than the graft material. All tensile strengths exceed this acceptance criterion.
Endoprosthesis Magnetic Resonance Imaging Evaluation	• MRI compatibility	The TAG device is not expected to present an additional hazard or risk when implanted in a patient subjected to MRI at 1.5-Tesla. There were no observable magnetic field interactions, minimal MRI-related heating (<1.0°C), and only minor image artifacts, meeting the acceptance criteria. The device has therefore been determined to be MRI-safe under these conditions.
Endoprosthesis Microscopic Determination of Porosity Test	• Permeability considerations • Patency of the implant	The fibril length of the ePTFE material comprising the luminal surface of the TAG device was determined. The acceptance criteria that the TAG device graft material meet the same fibril length criteria as the commercially available GORE-TEX Vascular Graft has been met.
Endoprosthesis Pulsatile Fatigue Test	• Durability and integrity of the implanted device	After 10 years simulated physiological loading of 400 million cycles, tested samples were examined visually and with magnification. There was no evidence of Nitinol wire pitting or cracking. Only a single fatigue-related fracture was identified. No significant wear, abrasion, or migration between the overlapping portion of devices was noted. The devices were intact after 10 years simulated *in vivo* physiological loading 400 million cycles with no perforation or detachment of the ePTFE graft as a result of pulsatile fatigue testing. The acceptance criteria that the modified TAG device perform equivalent or better than the original device was met.
Endoprosthesis Radial Force Test	• Fixation effectiveness of the implant • Appropriate Sizing of the implant • Patency of the implant	The radial forces of the TAG device were characterized at appropriate diameters representative of clinically relevant oversizing. The radial forces of the TAG device are anticipated to be adequate for clinical use. Clinical results to-date indicate acceptable radial force characteristics. The acceptance criteria that the modified TAG device perform equivalent or better than the original device was met.
Endoprosthesis Separation Force	• Testing of the modularity of the endovascular system (overlapped endoprostheses)	This test was performed for characterization purposes. The force required to separate overlapping TAG devices in an *in vitro* setting were characterized and found to be 70 - 350 gr under the un-pressurized test conditions. The separation (pull-out) force is expected to be sufficient for clinical use. Clinical results to-date indicates acceptable overlapped device separation force with no incidents of overlapped device separation.
Endoprosthesis Water Permeability Test	• Permeability considerations	Water permeability testing of the TAG endoprosthesis indicates that the water permeability of the modified TAG device is lower than the original TAG devices (8.05 vs 17.7 ml/min, respectively).
Endovascular System Simulated Use Test	• Ability to deploy the implant • Ability to accurately deploy • Fixation effectiveness of the implant	Deployment accuracy and resistance to migration of the TAG device was demonstrated under simulated flow conditions when used in a manner consistent with those set forth in the instructions for use (over-sizing, appropriate device placement, post-deployment balloon touch-up). In straight and angulated segments of a test model, at a 95% confidence level, the TAG endoprosthesis deployed within 5mm proximal of the intended implant site. The original and modified devices were tested and the modified device performed equivalent or better than the original device, meeting the acceptance criteria.
Graft Material Abrasion Test	• Durability and integrity of the implant • Testing of the modularity of the endovascular system	TAG graft material was compared to the original graft material in an abrasion test based upon ASTM methods. The results indicate that the modified graft material is more abrasion resistant than the control material (2601.4 vs 299.8 average cycles to failure, respectively). The acceptance criteria that the modified TAG device performs better than the original device was met.
Graft Material Water Entry Pressure Testing	• Permeability considerations	All graft material used in the manufacture of the TAG endoprosthesis is currently subjected to 100% water entry pressure testing during manufacturing. Materials that pass this test meet the acceptance criterion that the graft material does not leak.
Nitinol Material Analysis Test	• Durability and integrity of the implanted device	The bulk material and surface of the Nitinol wire used for the TAG device was chemically analyzed and quantified. Acceptance criteria include composition that meets material specifications and a consistently smooth wire surface with no unacceptable anomalies such as pitting, cracks, or contaminants. The surfaces of the wire were . examined under SEM to detect defects and contamination. The bulk material analysis and surface analysis met the acceptance criteria. Surface observations with SEM demonstrated a consistently smooth wire surface with no unacceptable anomalies such as pitting, cracks, or contaminants.

Shelf Life Testing

The GORE TAG Thoracic Endoprosthesis is a single-use device that is provided sterile to the end user. Sterilization validation for the TAG device demonstrates a Sterility Assurance Level (SAL) of 10^{-6}. Product and package stability testing of the GORE TAG Thoracic Endoprosthesis was performed and validated for a 3-year shelf life.

Animal Studies

Two animal studies were conducted in the development of the GORE TAG Thoracic Endoprosthesis (**Table 8**). Both studies were conducted with an ovine model using full scale devices. The first study (N = 15) evaluated the original TAG device and the second study (N = 21) utilized the modified TAG device in single and overlapping configurations. Follow-up times for these studies included 30, 60, 90 and 180 days post-treatment. The results of these studies demonstrated that the endoprosthesis was easy to introduce, visualize, and accurately deploy within the normal aorta. The host vascular response was good with no adverse biological reaction. Furthermore, no significant nitinol or ePTFE wear was observed from the in vivo environment at 6 months that compromised endoprosthesis performance.

Table 8. Summary of Animal Studies

Animal Study	#/Type of animal	Methods	Results/Conclusions
Acute, sub-chronic and chronic study of the original TAG device	15/ovine	Angiography and intravascular ultrasound (IVUS) were used to determine device size and location for implantation. Delivery performance was measured including compatibility with introducer sheath, guidewire and balloon catheter. Angiography, radiography and IVUS imaging modalities were used to evaluate the functional performance and luminal patency of the endoprosthesis. Implants were retrieved at 30, 60, 90 and 180 days post-operatively. Gross and histological examinations of the explants were performed.	Fourteen (14) of 15 devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device migration or graft disruption.
Acute, sub-chronic and chronic study of the modified TAG device	21/ovine	Angiography and IVUS were used to determine device size and location for implantation. Delivery performance was measured including compatibility with introducer sheath, guidewire and balloon catheter. Angiography, radiography and IVUS imaging modalities were used to evaluate the functional performance and luminal patency of the endoprosthesis. Implants were retrieved at 30, 60, 90 and 180 days post-operatively. Gross and histological examinations of the explants were performed.	All devices were successfully delivered and deployed. The functional requirements of the device were met and the devices performed as intended. All devices were patent at retrieval and the host tissue response was judged to be acceptable at both gross and histological examination. There was no evidence of device migration or graft disruption.

Clinical Studies

Two U.S. clinical studies were conducted to evaluate the safety and effectiveness of the GORE TAG Thoracic Endoprosthesis. The first, referred to as TAG 99-01, evaluated the original design. The second U.S. clinical study, referred to as TAG 03-03, evaluated a modified version of the device. This Summary of Safety and Effectiveness contains the results of both of these U.S. clinical studies. The data from these studies were not pooled for the purpose of analysis. The first study demonstrated the one-year safety and effectiveness of the GORE TAG Thoracic Endoprosthesis. The second study demonstrated that the changes in the device did not adversely affect the clinical performance of the device. The study was focused on 30 day follow-up, as the device changes were only likely to affect deployment and also because the majority of device events in the first study occurred within the first 30 days.

TAG 99-01 Summary

TAG 99-01 was a non-randomized, multi-center clinical study designed to compare subjects treated with endovascular repair to an open surgical repair control group for repair of aneurysms of the descending thoracic aorta (DTA). Seventeen U.S. sites enrolled 140 GORE TAG Thoracic Endoprosthesis and 94 surgical control subjects. GORE TAG Thoracic Endoprosthesis and Surgical Control subjects were required to meet the same inclusion/exclusion criteria with the exception of the anatomical criteria required for endovascular repair. The control group included both historical (50) and concurrent (44) surgical subjects; an analysis showed comparability between the two groups of surgical control subjects.

The subjects were assessed at pre-treatment, treatment, and hospital discharge and returned for follow-up visits at 1, 6, 12, and 24 months, with additional visits scheduled for 36, 48, and 60 months post-treatment. Subject follow-up and accountability at 1 month, 6 months, 12 months and 24 months are presented in **Table 9**.

An imaging core laboratory provided an independent assessment of the imaging data collected during this study. Site evaluation is presented in this summary because the study hypotheses required an evaluation of the clinical significance of adverse events (i.e., major vs minor). All clinical events were adjudicated by a clinical events committee, and safety was monitored by a data safety monitoring board.

The primary objective of the study was to evaluate the safety and effectiveness of endovascular repair with the original GORE TAG Thoracic Endoprosthesis as an alternative to open surgical repair. Safety was determined by comparing the proportion of subjects who experienced ≥ 1 major adverse event (MAE) through 12 months post-treatment between TAG 99-01 Test and TAG 99-01 Control subjects. Effectiveness was determined by evaluating the proportion of TAG 99-01 Test subjects free from a major device-related event through the 12-month follow-up visit in comparison to a predefined rate of success. Secondary objectives included an assessment of clinical benefit and quality-of-life measures.

TAG 03-03 Summary

After completion of enrollment in TAG 99-01, breaks in the wire frame were identified. Modifications were made to the device to allow for removal of the component associated with the fractures. A risk analysis determined that modifications could potentially affect the deployment of the device. As such, TAG 03-03 was designed to confirm that the modifications did not adversely affect the perioperative (through 30 days) performance of the GORE TAG Thoracic Endoprosthesis.

The TAG 03-03 study enrolled 51 subjects who underwent endovascular repair at 11 investigational sites. The TAG 99-01 surgical group served as the control. To support the comparability of the data between studies, the TAG 99-01 and TAG 03-03 studies used the same Inclusion/Exclusion criteria, screening assessments, clinical events committee, and imaging core laboratory. In addition, both studies collected identical study data (e.g., adverse events, device events).

Safety was determined by comparing the proportion of subjects who experienced ≥ 1 MAE through 30 days post-treatment between TAG 03-03 device subjects and TAG 99-01 Control subjects. Efficacy was the proportion of subjects who experienced ≥ 1 major device-related event in TAG 03-03 Test subjects through the 30-day follow-up visit. Efficacy data are presented descriptively. Secondary objectives included an assessment of clinical benefits and quality-of-life measures.

Table 9. Subject Status Through 24 Months

Subject disposition category*	Follow-up period								
	1 month			6 months		12 months		24 months	
	TAG 99-01 (N=140)	TAG 99-01 Control (N=94)	TAG 03-03 (N=51)	TAG 99-01	TAG 99-01 Control	TAG 99-01	TAG 99-01 Control	TAG 99-01	TAG 99-01 Control
Available for visit	133	78	51	116	69	104	65	92	56
Expired[2]	3	13	0	19	19	28	22	36	26
Withdrew or lost to follow-up[2,3]	4	3	0	5	6	8	7	12	12
Missed visit	12	19	3	15	25	2	13	8	10
Had a follow-up visit within window[1]	121	59	48	101	44	102	52	84	46
Had a follow-up visit outside window[1]	7	17	n/a	4	3	1	4	1	6
CT imaging	110	12	48	100	15	103	34	80	27
X-ray imaging	24	26	48	76	7	88	8	75	11
Site evaluated for endoleak	110	n/a	48	100	n/a	103	n/a	80	n/a
Site evaluated for aneurysm enlargement[4]	n/a	n/a	n/a	83	n/a	85	n/a	69	n/a

* Categories are mutually exclusive and exhaustive. Each successive category does not include subjects from the previous category.

[1] Data not included in study analyses.

[2] Cumulative; includes subjects from study start to end of indicated period.

[3] If subject withdrew and had a follow-up visit within the same period, subject is included as having had a follow-up visit for that period. Subject is counted as withdrawn in the following period.

[4] Aneurysm enlargement was evaluated for patients with adequate paired CT images.

Patient Demographics and Pretreatment History (TAG 99-01 & TAG 03-03)

Tables 10 - 12 compare subjects receiving the TAG Endoprosthesis (TAG 99-01 & TAG 03-03) and open surgical repair subjects.

Table 10. Subject Demographics

Variable	TAG 03-03 (N = 51)	TAG 99-01 (N = 139)	Surgical 99-01 (N = 94)	TAG 03-03 vs. TAG 99-01 p-value[1]	TAG 03-03 vs. Surgical 99-01 p-value[1]
Gender, n (%)				0.41	0.12
Female	18 (35)	59 (42)	46 (49)		
Male	33 (65)	80 (58)	48 (51)		
Age (years)	70.7 ± 9.4	70.4 ± 10.5	68.2 ± 10.2	0.88	0.15
Ethnicity, n (%)				0.66	0.77
Asian	1 (2)	1 (1)	2 (2)		
Black	2 (4)	11 (8)	9 (10)		
Caucasian	47 (92)	121 (87)	81 (86)		
Hispanic	1 (2)	3 (2)	1 (1)		
Other	0 (0)	3 (2)	1 (1)		
Weight (kg)	80.8 ± 20.5	76.5 ± 16.5	77.6 ± 17.5	0.14	0.34
Height (cm)	171.0 ± 10.6	169.6 ± 10.1	169.5 ± 11.3	0.39	0.44
BMI (kg/m^2)	27.5 ± 5.7	26.5 ± 4.7	26.9 ± 5.0	0.22	0.54

Notes: Denominators are the number of subjects who have each specific baseline variable available.
[1] p-values are based on Fisher's exact test for categorical variables and a two-sample t-test for continuous variables.

Table 11. Comparison of Subject Pre-treatment Medical History

Variable	TAG 03-03 (N = 51) n (%)	TAG 99-01 (N = 139) n (%)	TAG 99-01 Control (N = 94) n (%)	TAG 99-01 vs. TAG 99-01 Control p-value[1]	TAG 03-03 vs. TAG 99-01 p-value[1]	TAG 03-03 vs. TAG 99-01 Control p-value[1]
Coronary artery disease	18 (35)	69 (50)	34 (36)	0.060	0.10	1.00
Cardiac arrhythmia	16 (31)	33 (24)	29 (31)	0.23	0.35	1.00
Valvular heart disease	5 (10)	8 (6)	9 (10)	0.45	0.34	1.00
Congestive heart failure	4 (8)	13 (9)	9 (10)	1.00	1.00	1.00
Stroke	4 (8)	14 (10)	9 (10)	1.00	0.78	1.00
Peripheral arterial occlusive disease (infrainguinal)	7 (14)	21 (15)	10 (11)	0.33	1.00	0.60
Prior vascular intervention	29 (57)	62 (45)	52 (55)	0.14	0.14	1.00
Thromboembolic event	4 (8)	10 (7)	6 (6)	1.00	1.00	0.74
Aneurysm symptomatic	13 (25)	30 (22)	36 (38)	0.007	0.56	0.14
Aneurysm of traumatic origin	2 (4)	8 (7)	5 (6)	1.00	0.73	0.71
Other concomitant aneurysm(s)	17 (33)	38 (27)	26 (28)	1.00	0.47	0.57
COPD	21 (41)	55 (40)	36 (38)	0.89	0.87	0.86
History of smoking (current or past)	43 (84)	116 (83)	77 (82)	0.86	1.00	0.82
Renal dialysis	2 (4)	2 (1)	0 (0)	0.52	0.29	0.12
Paraplegia	0 (0)	1 (1)	0 (0)	1.00	1.00	N/A[2]
Erectile dysfunction	1 (3)	13 (16)	5 (10)	0.44	0.063	0.39
Hepatic dysfunction	2 (4)	3 (2)	1 (1)	0.65	0.61	0.28
Bleeding disorder(s)	2 (4)	4 (3)	5 (5)	0.49	0.66	1.00
Cancer	16 (31)	27 (19)	12 (13)	0.21	0.12	0.009

Table 11 (continued)

Variable	TAG 03-03 (N = 51) n (%)	TAG 99-01 (N = 139) n (%)	TAG 99-01 Control (N = 94) n (%)	TAG 99-01 vs. TAG 99-01 Control p-value[1]	TAG 03-03 vs. TAG 99-01 p-value[1]	TAG 03-03 vs. TAG 99-01 Control p-value[1]
NYHA classification[3]						
I	21 (55)	39 (48)	22 (46)			
II	14 (37)	35 (43)	14 (29)			
III	3 (8)	7 (9)	12 (25)			
N/A	13 (25)	58 (42)	46 (49)			
ASA classification				0.13	0.41	0.29
I	3 (6)	2 (1)	2 (2)			
II	4 (8)	13 (9)	5 (5)			
III	31 (61)	90 (65)	51 (54)			
IV	13 (25)	34 (24)	36 (38)			
Summary of mean SVS risk scores	0.7 ± 0.4	0.7 ± 0.3	0.6 ± 0.3	0.17	0.24	0.38

Note: Denominators are the number of subjects with known observations for each specific baseline variable.
For N/A values, denominators are the number of subjects enrolled.

[1] p-values are based on Fisher's exact test for categorical variables and a two-sample t-test for the risk summary score.

[2] Not evaluable using Fisher's exact test.

[3] NYHA was used to exclude Class IV patients from the studies and not to compare the distribution of the classification among groups.

Table 12 lists the initial aneurysm diameter sizes treated.

Table 12. Aneurysm Diameter Distribution

Diameter Range	TAG 99-01 N=140 n (%)	TAG 99-01 Surgical N=94 n (%)	TAG 03-03 N=51 n (%)
10 – 19 mm	0	1 1%	0
20 – 29 mm	1 1%	1 1%	0
30 – 39 mm	7 5%	3 4%	0
40 – 49 mm	18 13%	5 6%	5 10%
50 – 59 mm	18 13%	17 20%	14 27%
60 – 69 mm	45 32%	30 35%	23 45%
70 – 79 mm	28 20%	16 19%	7 14%
80 – 89 mm	15 11%	8 9%	0
90 – 99 mm	5 4%	2 2%	1 2%
100 – 109 mm	1 1%	1 1%	1 2%
110 – 119 mm	1 1%	1 1%	0

Results

The primary and secondary objectives of TAG 99-01 and TAG 03-03 trials were met. Subjects treated with the GORE TAG Thoracic Endoprosthesis experienced a greater probability of remaining free from a MAE than subjects treated with open surgical repair. In addition, data from the TAG 99-01 and TAG 03-03 studies demonstrated that the GORE TAG Thoracic Endoprosthesis subjects experienced a low incidence of major device-related events. Also, subjects treated with the endoprosthesis experienced less blood loss during the procedure, shorter ICU stay, shorter hospital stay and shorter time to return to normal daily activities than subjects treated with open surgical repair. The detailed results are separated into Safety, Efficacy and Secondary endpoints.

Table 13 lists the number of devices implanted for TAG 99-01 and TAG 03-03. More than 50% of subjects required more than one device (**Table 14**). Some subjects had more than one size device implanted.

Table 13. Devices Implanted

Endoprosthesis Diameter (mm)	TAG 99-01 Number of devices (N = 234) n (%)	TAG 03-03 Number of devices (N = 93) n (%)
26	9 (4)	2 (2)
28	9 (4)	6 (6)
31	32 (14)	11 (12)
34	102 (44)	28 (30)
37	41 (18)	26 (28)
40	41 (18)	20 (22)

Table 14. Number of Endoprostheses Implanted at Initial Procedure

Number of devices implanted	TAG 99-01 Number of subjects (N = 137*) n (%)	TAG 03-03 Number of subjects (N = 51) n (%)
1	61 (45)	17 (33)
2	60 (44)	26 (51)
3	11 (8)	8 (16)
4	5 (4)	0

* There were three patients with access failures who did not receive a device.

Safety

The primary safety endpoint for the Pivotal Study, the proportion of subjects who experienced ≥ 1 MAE through 1 year post-treatment, was significantly lower ($p < 0.001$) in the TAG 99-01 device (42%) vs. the TAG 99-01 surgical control (77%) group. The incidence of major bleeding (11% vs. 54%), pulmonary (13% vs. 38%), renal (4% vs. 15%), wound (6% vs. 15%), and neurological (11% vs. 33%) complications was lower in the TAG 99-01 device group through 1 year post-treatment. Among the clinically significant major neurologic complications, 4/140 (3%) in the TAG 99-01 device group and 13/94 (14%) in the TAG 99-01 surgical control group experienced paraplegia or paraparesis.

Tables 15–20 and **Figures 3-7** describe the morbidity and mortality outcomes for TAG 99-01 and TAG 03-03. The GORE TAG Thoracic Endoprosthesis subjects experienced significantly less major adverse events for both TAG 99-01 and TAG 03-03. Aneurysm related mortality is also less in the GORE TAG Thoracic Endoprosthesis group. All-cause mortality is not different between the GORE TAG Thoracic Endoprosthesis and surgical control.

Table 15: Summary of Kaplan-Meier Curves to 24 Months

	Total Number of Patients Reaching Follow-up			Aneurysm Rupture		Conversion to Surgical Repair	Death		Aneurysm Related Death[1]		Major Adverse Event	
	T1 N	C N	T2 N	T1 N	C N	T1 N	T1 N %	C N %	T1 N %	C N %	T1 N %	C N %
Intra-operative	140	94	51	0	0	0	0	0	0	0	n/a[2]	n/a[2]
≤ 30 Days	133	78	48	0	0	0	2 2%	6 5%	2 2%	6 5%	40 29%	66 47%
> 30 Days to 12 Months	104	65	n/a	0	0	0	22 21%	14 13%	2 2%	3 3%	19 18%	6 6%
12 Months to 24 Months	92	56	n/a	0	0	0	10 11%	4 4%	0	0	9 10%	1 1%
Total Patients	140	94	51	0	0	0	34	24	4	9	68	6
Kaplan-Meier Summaries				Freedom from Aneurysm Rupture		Freedom from Conversion	Probability of Survival		Freedom from Aneurysm Related Death		Freedom from Major Adverse Event	
12 Month Kaplan-Meier	104	65	n/a	100%	100%	100%	82%	78%	97%	90%	57%[3]	23%[3]
24 Month Kaplan-Meier	92	56	n/a	100%	100%	100%	74%	72%	97%	90%	50%[3]	21%[3]

T1 = TAG 99-01

C = TAG 99-01 Control

T2 = TAG 03-03

[1] Aneurysm related death is defined as all deaths due to aneurysm rupture, a primary or secondary procedure, surgical conversion, or within 30 days of the primary or secondary procedure.

[2] Major adverse events during the intraoperative period are reported in the ≤30 day period.

[3] Total number of patients with a first adverse event only.

Figure 3. Subjects Free of a Major Adverse Event (TAG 99-01)

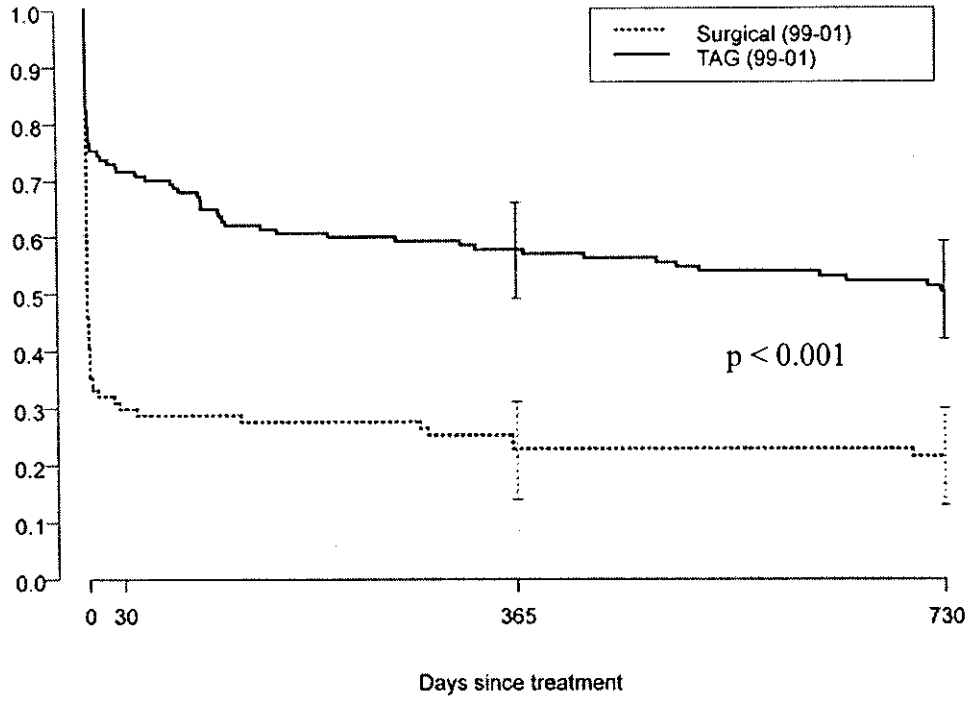

Table 16. Subjects Free of a Major Adverse Event (TAG 99-01)

	Test (N=140)		Control (N= 94)		Probability of remaining event-free from Day 0	
Days from treatment[1]	Number event-free at start of interval	Number with event	Number event-free at start of interval	Number with event	Test	Control
[0, 30]	140	40	94	66	0.71	0.30
(30, 182]	98	15	27	2	0.60	0.27
(182, 365]	83	4	24	4	0.57	0.23
(365, 730]	76	9	19	1	0.50	0.21

[1] (lower endpoint, upper endpoint] denotes > lower endpoint and <= upper endpoint.
Note: Column header are the number of subjects enrolled. Probability of remaining event-free is the Kaplan-Meier estimate.

Figure 4. Subjects Free of a Major Adverse Event (TAG 03-03)

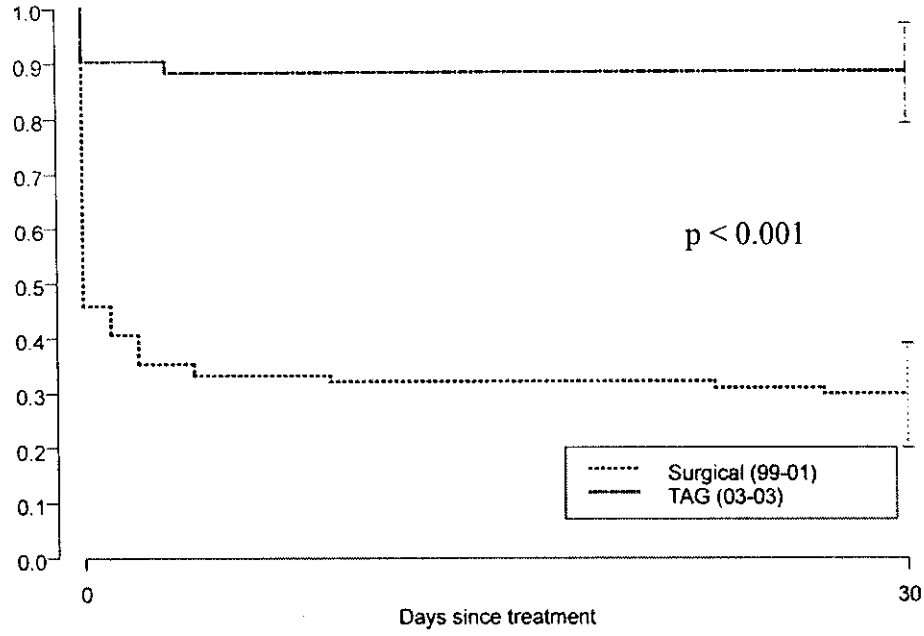

Table 17. Subjects Free of a Major Adverse Event (TAG 03-03)

	TAG 03-03 (N= 51)		TAG 99-01 Control (N= 94)		Probability of remaining event-free from Day 0	
Days from treatment[1]	Number event-free at start of interval	Number with event	Number event-free at start of interval	Number with event	TAG 03-03	TAG 99-01 Surgical
[0, 30)	51	6	94	66	0.88	0.30

[1] [lower endpoint, upper endpoint) denotes >= lower endpoint and < upper endpoint.
Note: Column header are the number of subjects enrolled. Probability of remaining event-free is the Kaplan-Meier estimate.

The proportion of TAG 99-01 and TAG 03-03 subjects that experienced ≥1 MAE through 30 days post treatment was less than TAG 99-01 surgical control subjects (**Fig. 5**).

Figure 5. Subjects Free of a Major Adverse Event Through 30-days Post-treatment

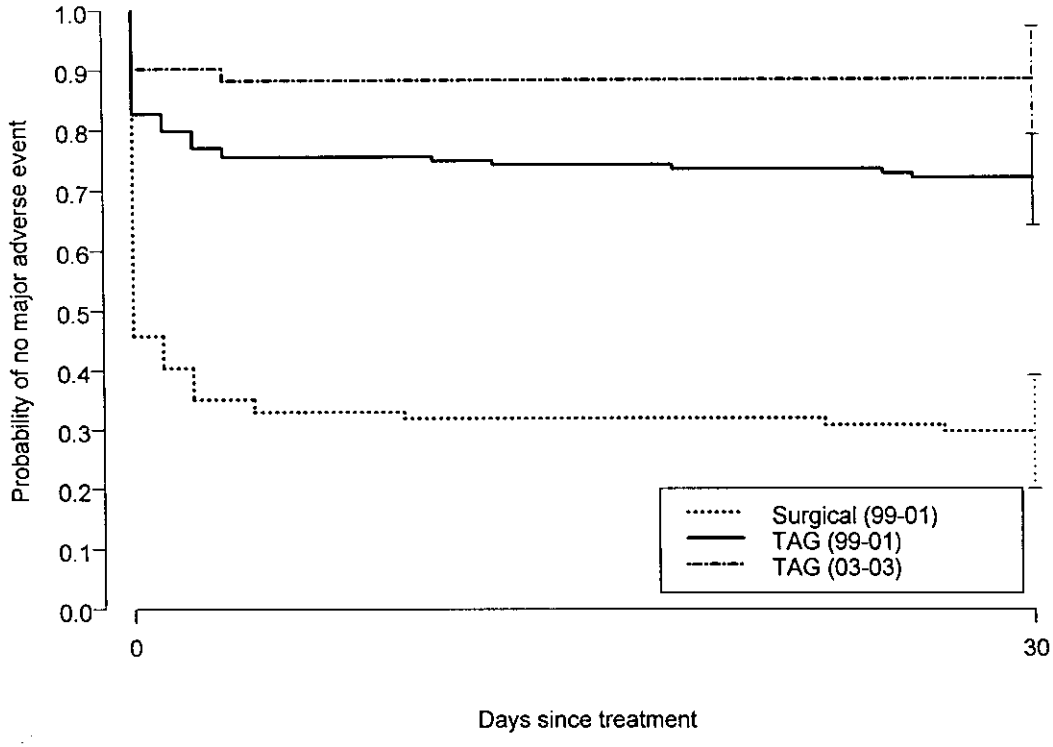

Table 18. Subjects Free of a Major Adverse Event Through 30 Days Post-treatment

Days from treatment[1]	Treatment group	Number event-free at start of interval	Number with event	Probability of remaining event-free from Day 0
[0, 30)	TAG 03-03 (N = 51)	51	6	0.88
[0, 30)	TAG 99-01 (N=139)	139	39	0.72
[0, 30)	TAG 99-01 Surgical (N=94)	94	66	0.30

Note: Probability of remaining event-free is the Kaplan-Meier estimate.
[1] [lower endpoint, upper endpoint) denotes >= lower endpoint and < upper endpoint.

Figure 6. Aneurysm-related Mortality Through 2 Years Post-treatment (TAG 99-01)

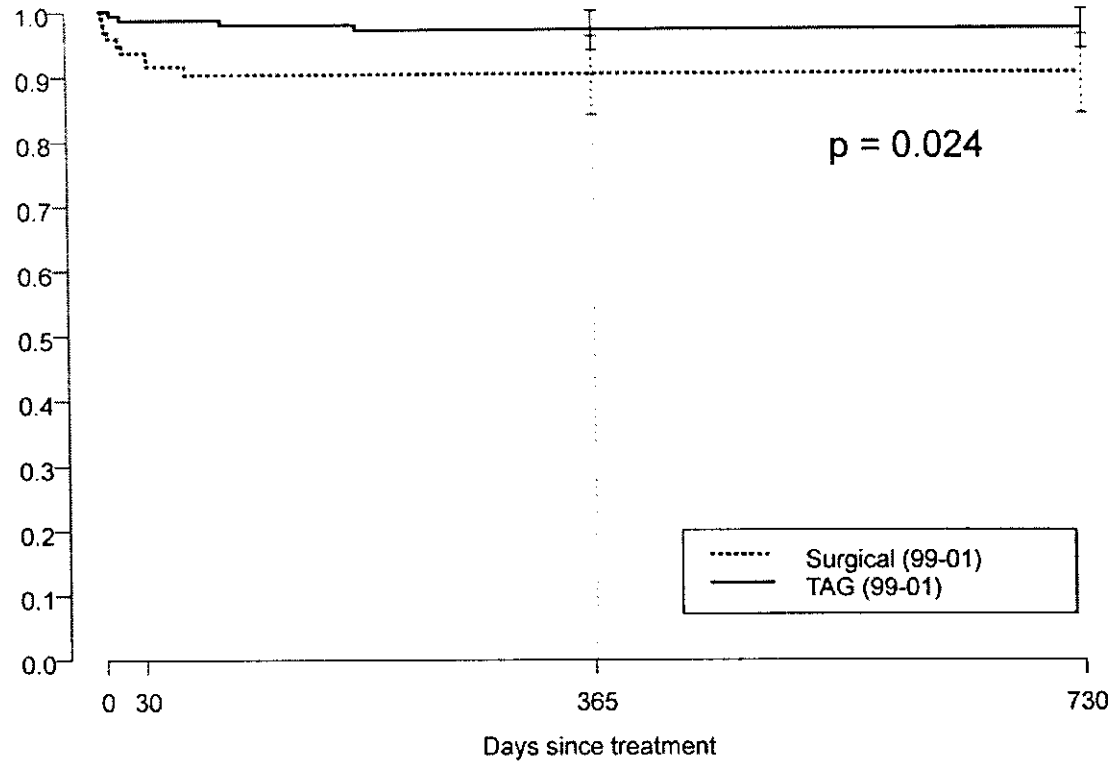

Table 19. Aneurysm-related Mortality Through 2 Years Post-treatment (TAG 99-01)

Days from treatment[1]	TAG 99-01 (N= 140)		TAG 99-01 Surgical (N= 94)		Probability of remaining alive from Day 0	
	Number alive at start of interval	Number died	Number alive at start of interval	Number died	TAG 99-01	TAG 99-01 Surgical
[0, 30]	140	2	94	6	0.99	0.94
(30, 182]	134	1	85	3	0.98	0.90
(182, 365]	120	1	66	0	0.97	0.90
(365, 730]	105	0	62	0	0.97	0.90

[1] (lower endpoint, upper endpoint] denotes > lower endpoint and <= upper endpoint.
Note: Column header are the number of subjects enrolled. Probability of remaining alive is the Kaplan-Meier estimate.

Figure 7. All-cause Mortality Through 2 Years Post-treatment (TAG 99-01)

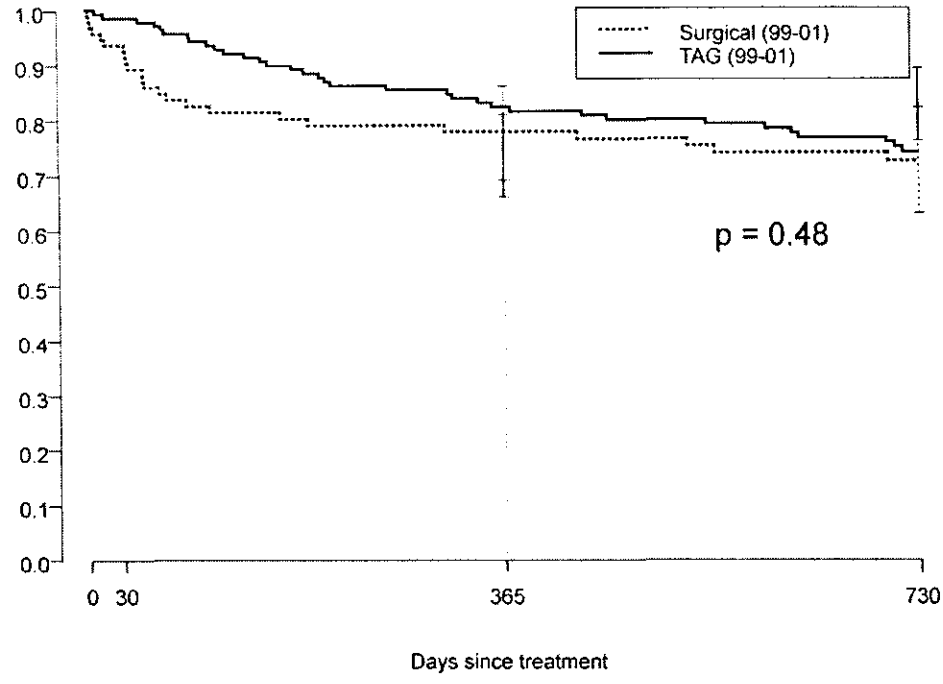

Table 20. All-cause Mortality Through 2 Years Post-treatment (TAG 99-01)

	TAG Device (N=140)		Surgical Control (N= 94)		Probability of remaining alive from Day 0	
Days from treatment[1]	Number alive at start of interval	Number died	Number alive at start of interval	Number died	TAG Device	Surgical Control
[0, 30]	140	2	94	6	0.99	0.94
[30, 182]	134	13	85	12	0.89	0.80
[182, 365]	120	9	66	2	0.82	0.78
[365, 730]	105	10	62	4	0.74	0.72

[1] (lower endpoint, upper endpoint] denotes > lower endpoint and <= upper endpoint.
Note: Column header are the number of subjects enrolled. Probability of remaining alive is the Kaplan-Meier estimate.

Efficacy

The primary efficacy outcome of this Pivotal Study was the proportion of subjects treated with the GORE TAG Thoracic Endoprosthesis free from a major device-related event through the 12-month follow-up visit as reported by the investigative sites. Since device-related events associated with endovascular therapy are different than those associated with open surgical repair, no meaningful efficacy comparisons may be made between the treatment groups.

An imaging core laboratory was used as part of TAG 99-01 to provide an independent assessment of the imaging data collected during this study. Computed tomography films (CTA/CT) and radiographs (X-Ray) for study subjects were sent from the investigative sites to the imaging core laboratory to assess aortic morphology, vascular characteristics, and device integrity. Categories for endoleak are not mutually exclusive and therefore numbers of specific endoleak types may add to more than the total patients with endoleak. An analysis of subjects with an endoleak present at 12 months identified 2 of 7 or 29% had aneurysm enlargement.

Table 21 summarizes site and core lab findings from TAG 99-01. The difference in observed endoleaks was a result of peri-procedural imaging which the core laboratory did not evaluate. The 6 additional wire-frame fractures and 1 additional migration identified by the core laboratory were not associated with clinical sequelae or reintervention. Site reported data for all other device-related events were worst case with respect to the number of events identified.

Table 21. Device-related Event Incidence: Core Lab and Site Data for Test Subjects Through the 12-month Follow-up Visit (TAG 99-01)

Device-related events	Core Lab TAG 99-01 (N=131) n (%)	Site TAG 99-01 (N = 140) n (%)
Endoleak (by CT)	**12/124 (10)[1]**	**22/140 (16)**
Type I	1/124 (1)	15/140 (11)
Ia (proximal)	n/a	14/140 (10)
Ib (distal)	n/a	2/140 (1)
Type II	1/124 (1)	3/140 (2)
Type III	0/124	3/140 (2)
Type IV	0/124	0/140
Indeterminate origin	10/124 (8)	4/140 (3)
Aneurysm rupture (by CT)	**0/124[1]**	**0/140**
Fracture (by x-ray)[3]	**7/126 (6)[1]**	**1/140 (1)**
Change in aneurysm diameter at 12 Month Visit from Month 1 visit (by CT)[2]		
Increase (≥ 5mm)	5 /81 (6)	8/83 (10)
No change (increase or decrease < 5mm)	55/81 (68)	40/83 (48)
Decrease (≥ 5mm)	21/81 (26)	35/83 (42)
Prosthesis migration (by CT)[4]	**2/124 (2)[1]**	**1/140(1)**

Notes: Denominators are N specified for each subject period from readable scans. A subject is counted at most once in period. Categories for endoleak are not mutually exclusive.

[1] N at each follow-up period is the number of subjects with evaluations of the specified complication (documented presence or absence) by the indicated modality (i.e., CT or x-ray).

[2] N at each follow-up period is the number of subjects with a complete data pair at both the Month 1 visit and the period indicated.

[3] All fractures identified were classified as minor

[4] All migrations identified were classified as minor

Tables 22 and **24** summarize all site reported device-related events. Site evaluation was used in the determination of efficacy because the study hypotheses required an evaluation of the clinical significance of device-related events (i.e., major vs minor).

Table 22 summarizes the incidence of major device-related events in the TAG 99-01 device group through the 12-month follow-up visit. The TAG Thoracic Endoprosthesis demonstrated a low rate of device complications in both TAG 99-01 and TAG 03-03 studies. Eight subjects (6%) experienced ≥ 1 major device-related event through the 12-month follow-up visit in TAG 99-01 and no subjects experienced major device-related events in TAG 03-03 through 30 days. The estimated 12-month freedom from a major device-related event was 0.94 in TAG 99-01. Only 1 additional major device-related event was reported from 12 to 24 months follow-up period of TAG 99-01. The definition of 'major' used for adverse events also applies to the device events used for the efficacy endpoint.

Table 22. Patients With Major Device-Related Events by Follow-up Periods (Site Reported)

Major device-related event[1]	Post-treatment follow-up period			
	Through Month 1 visit		> Month 1 visit to Month 12 visit	> Month 12 visit to Month 24 visit
	TAG 99-01 (N = 140) n (%)	TAG 03-03 (N = 51) n (%)	TAG 99-01 (N = 131) n (%)	TAG 99-01 (N = 100) n (%)
Any major device-related event	**6 (4)**	**0**	**2 (2)**	**1 (1)**
Endoleak	**3 (2)**	**0**	**1 (1)**	**0**
Type I	2 (1)	0	1 (1)	0
Ia (proximal)	2 (1)	0	1 (1)	0
Ib (distal)	0	0	0	0
Type II	0	0	0	0
Type III	0	0	0	0
Type IV	0	0	0	0
Indeterminate	1 (1)	0	0	0
Aneurysm rupture	**0**	**0**	**0**	**0**
Treatment-related device event	**2 (1)**	**0**	**0**	**0**
Access failure	0	0	0	0
Deployment failure	1 (1)	0	0	0
Other device complication	1 (1)	0	0	0
Unplanned occlusion of a branch vessel	**1 (1)**	**0**	**0**	**0**
Left subclavian	0	0	0	0
Left carotid	0	0	0	0
Celiac axis[3]	1 (1)	0	0	0
Renal[3]	1 (1)	0	0	0
Superior mesenteric[3]	1 (1)	0	0	0
Non-specified	0	0	0	0
Lumen obstruction	**0**	**0**	**0**	**0**
Prosthesis migration	**0**	**0**	**1 (1)**	**0**
Prosthesis realignment	**0**	**0**	**0**	**0**
Fracture	**0**	**0**	**0**	**0**
Aneurysm enlargement[4]	**1 (1)**	**0**	**2 (2)**	**1 (1)**
Extrusion / erosion	**0**	**0**	**0**	**0**
Other device complication after treatment	**0**	**0**	**0**	**0**

[1] All events are based on the Sacks criteria for a major event.
[2] One right external iliac rupture during sheath removal.
[3] Occurred in same patient
[4] Aneurysm enlargement is based on a change >= 5 mm from the Month 1 visit or the most recent scan.

Six subjects (4%) treated with the TAG Thoracic Endoprosthesis required implantation of an additional TAG Thoracic Endoprosthesis to treat the aneurysm through 1 year post-treatment. The reasons for these interventions are listed in **Table 23**.

Table 23. Reasons for Implantation of Additional Devices

Reason for intervention	Number of patients
Deployment failure	1
Endoleak	1
Aneurysm Enlargement	1
Endoleak and Aneurysm Enlargement	2
Endoleak, Aneurysm Enlargement and Prosthesis Migration	1
TOTAL	**6**

Table 24 lists the minor device-related events for both the TAG 99-01 and TAG 03-03 device subjects. The majority of the minor device-related events in TAG 99-01 device subjects occurred in the first 30 days. Only 2% of patients experienced a minor device-related event between 1 month and 12 months and only 4% experienced a minor device-related event between 12 months and 24 months.

Table 24. Minor Device-related Events, Day 0 Through Month 24 Visit, Site-reported

Minor device-related event	Post-treatment follow-up period			
	Through Month 1 visit		> Month 1 visit to Month 12 visit	> Month 12 visit to Month 24 visit
	TAG 99-01 (N = 140) n (%)	TAG 03-03 (N = 51) n (%)	TAG 99-01 (N = 131) n (%)	TAG 99-01 (N = 100) n (%)
Any minor device-related event	**22 (16)**	**10 (20)**	**2 (2)**	**4 (4)**
Endoleak	**19 (14)**	**6 (12)**	**1 (1)**	**2 (2)**
Type I	11 (8)	4 (8)	1 (1)	0
Ia (proximal)	10 (7)	3 (6)	1 (1)	0
Ib (distal)	2 (1)	1 (2)	0	0
Type II	3 (2)	2 (4)	0	1 (1)
Type III	3 (2)	0	0	1 (1)
Type IV	0	0	0	0
Indeterminate	3 (2)	0	0	0
Treatment-related device event	**4 (3)**	**3 (2)**	**0**	**0**
Access failure	1 (1)	0	0	0
Deployment failure	0	0	0	0
Other device complication at treatment	3 (2)	3 (2)	0	0
Unplanned occlusion of a branch vessel	**1 (1)**	**1 (1)**	**0**	**0**
Left subclavian	0	0	0	0
Left carotid	0	0	0	0
Renal	1 (1)	1 (1)	0	0
Non-specified	0	0	0	0
Lumen obstruction	**0**	**0**	**0**	**1 (1)**
Prosthesis migration	**1 (1)**	**1 (1)**	**0**	**0**
Prosthesis realignment	**0**	**0**	**0**	**0**
Prosthesis material failure	**0**	**0**	**1 (1)**	**1 (1)**
Extrusion / erosion	**0**	**0**	**0**	**0**
Other device complication after treatment	**0**	**0**	**0**	**0**

Secondary Endpoints

Table 25 describes the peri-procedural secondary endpoints for TAG 99-01 and TAG 03-03 Test subjects as well as TAG 99-01 Control subjects. The GORE TAG Thoracic Endoprosthesis groups had improved clinical benefit over the surgical control with respect to blood loss, length of ICU and hospital stay and the time to return to normal activities.

Table 25. Secondary Endpoints

Endpoint	TAG 03-03	TAG 99-01	TAG 99-01 Control	TAG 99-01 vs. TAG 99-01 Control p-value[1]	TAG 03-03 vs. TAG 99-01 Control p-value[1]
Blood loss during procedure (ml)	222.4 ±198.0 (n = 51)	471.9 ±862.7 (n = 132)	2402 ± 2719 (n = 52)		
Length of ICU stay (days)	1.2 ± 1.3 (n = 51)	2.7 ± 14.6 (n = 136)	5.2 ± 7.2 (n = 91)	< 0.001	< 0.001
Length of hospital stay (days)	4.8 ± 5.0 (n = 51)	7.4 ± 17.7 (n = 139)	14.4 ± 12.8 (n = 91)	< 0.001	< 0.001
Time to return to normal daily activities (days)	18.5 ± 15.9 (n = 42)	60.2 ± 82.7 (n = 114)	149.2 ±201.0 (n = 51)		

[1] no test of significance due to high proportion of surgical (TAG 99-01) missing data.

Conclusions

Data from TAG 99-01 and TAG 03-03 studies provide a reasonable assurance of safety and effectiveness of the GORE TAG Thoracic Endoprosthesis for the treatment of aneurysms of the descending thoracic aorta. Subjects treated with the GORE TAG Thoracic Endoprosthesis experienced a greater probability of remaining free from MAEs than subjects treated with open surgical repair. In addition, data from the TAG 99-01 and TAG 03-03 studies suggest that GORE TAG Thoracic Endoprosthesis subjects experienced a low incidence of major device-related events. Also, subjects treated with the endoprosthesis experienced less blood loss during the procedure, shorter ICU stay, shorter hospital stay and shorter time to return to normal daily activities than subjects treated with open surgical repair. Results from the TAG 03-03 study confirmed that the device modifications did not adversely affect clinical outcomes.

Panel Recommendation

The GORE TAG Thoracic Endoprosthesis was presented to the Circulatory System Device Panel on January 13, 2005. The Panel recommended approving the device with conditions. The first condition is a post approval study with an appropriate number of patients, five year follow-up, power to look at endpoints of mortality, aneurysm rupture, and paraplegia. The second condition is appropriate training. The last condition is adding specific inclusion/exclusion criteria from the studies to the indication, specifically the anatomical criteria.

FDA Decision

FDA reviewed portions of the Premarket approval (PMA) application under the modular PMA process (M030017). All of the modules were incorporated into the review of the PMA (P040043).

FDA concurred with the Circulatory System Devices Panel recommendations of January 13, 2005. To address these conditions, W. L. Gore & Associates submitted: 1) a written concurrence to conduct a five year follow up post market study; 2) developed a physician training program; and 3) revised the labeling to address the concerns raised by the panel, which was reviewed by FDA and found acceptable.

FDA issued an approval order for P040043 on March 23, 2005. The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 814).

Approval Specifications

Directions for Use

See Labeling.

Hazards to Health from Use of the Device

See Indications, Contraindications, Warnings, Precautions and Adverse Events in the Labeling.

Post-approval Requirements, Restrictions

See approval order.