TMM: Note that the font will be edited for the final print

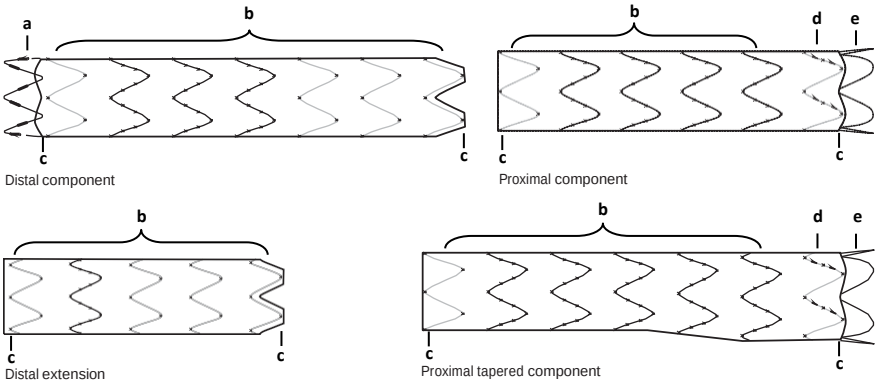
Clinical Summary is a separate document and will be made available online.

Zenith Alpha™ Thoracic Endovascular Graft

Instructions for Use

Patient I.D. Card Included

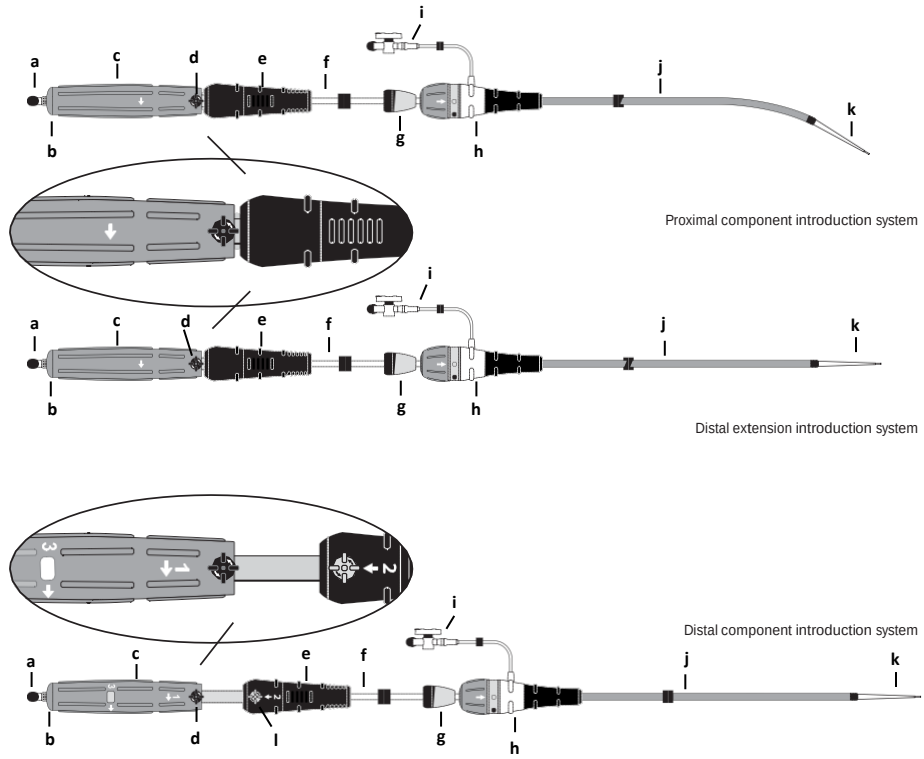
TABLE OF CONTENTS



1

Stent Graft Components

a. Distal bare stent with barbs
b. Body stent (internal or external)
c. Gold radiopaque markers (located near stent apices on proximal and distal edges of graft)
d. Proximal sealing stent with barbs
e. Bare alignment stent

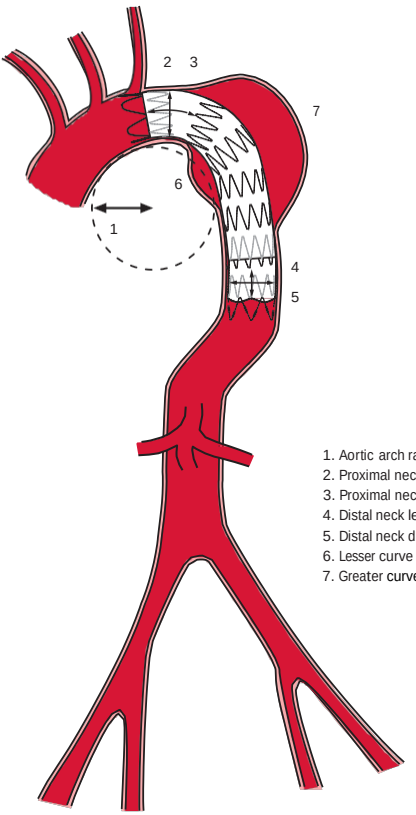


l_2

Introduction System Components

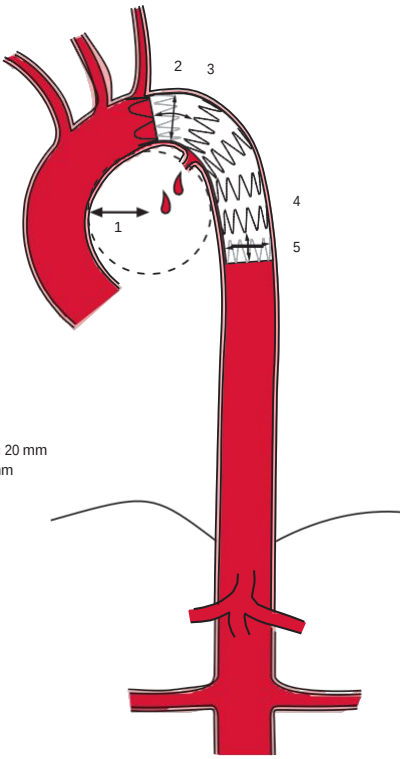
a. Cannula hub
b. Back-end cap
c. Blue rotation handle
d. Black safety-lock knob
e. Black gripper (telescoping on distal component)
f. Gray positioner
g. Captor sleeve
h. Captor hemostatic valve
i. Connecting tube with stopcock
j. Flexor sheath
k. Dilator tip
l. Gray safety-lock knob

3

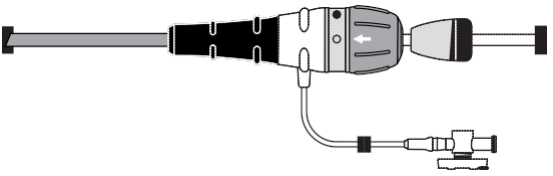


1. Aortic arch radius of curvature ≥ 20 mm
2. Proximal neck diameter 15-42 mm
3. Proximal neck length ≥ 20 mm
4. Distal neck length ≥ 20 mm
5. Distal neck diameter 15-42 mm
6. Lesser curve
7. Greater curve

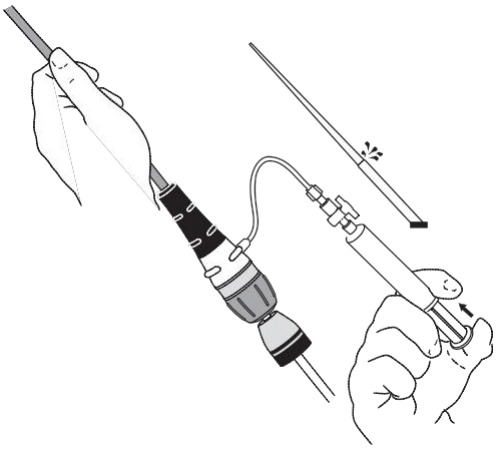
3



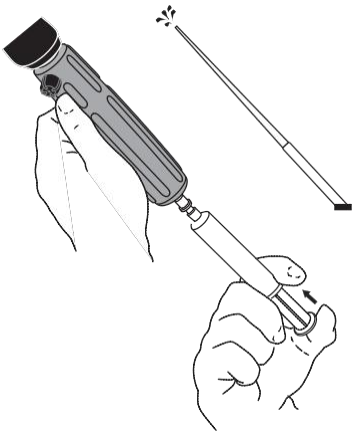
4



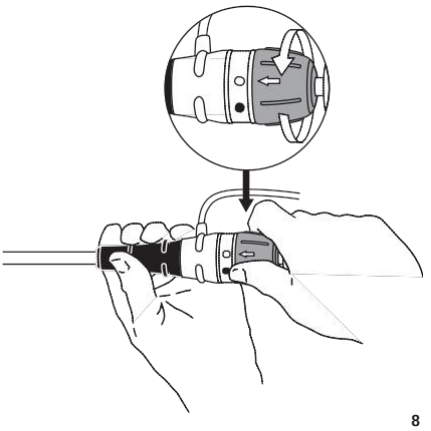
5



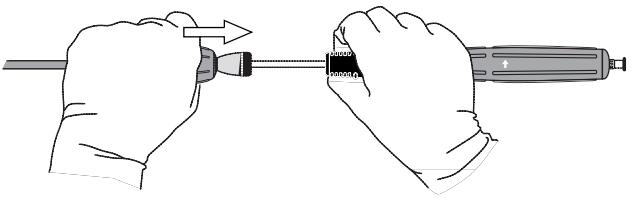
6



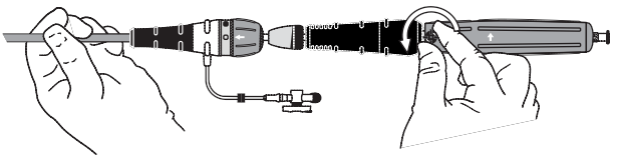
7



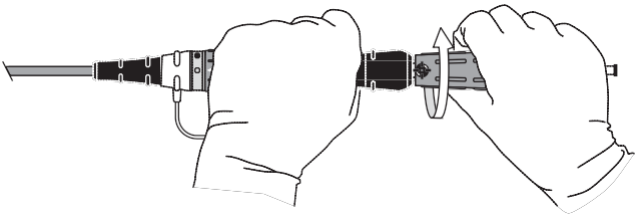
8



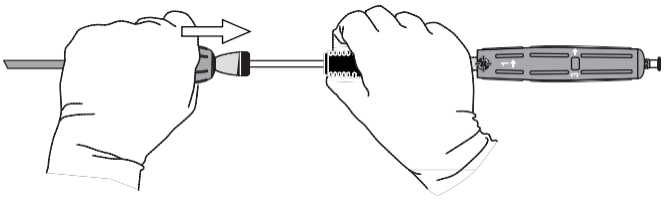
9



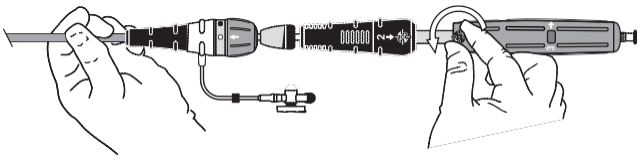
10



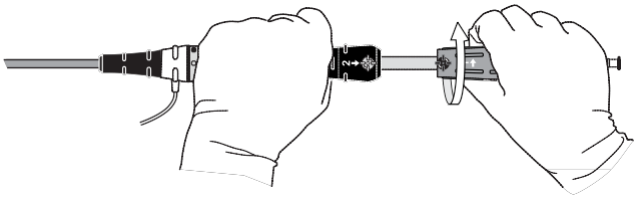
11



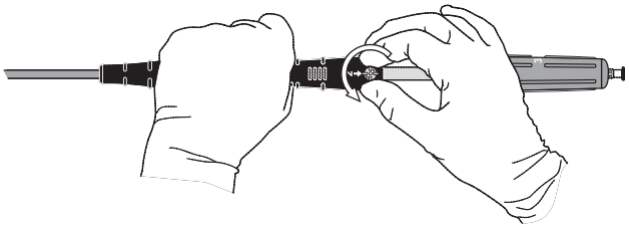
12



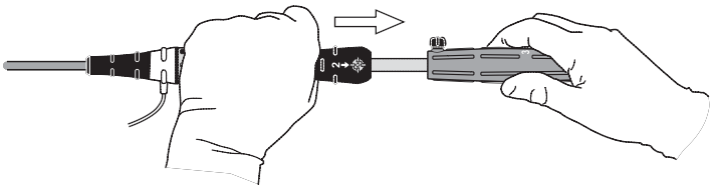
13



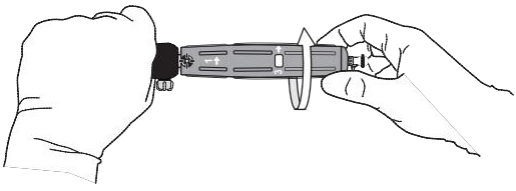
14



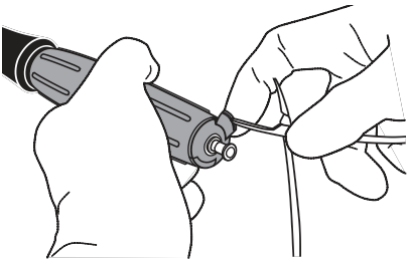
15



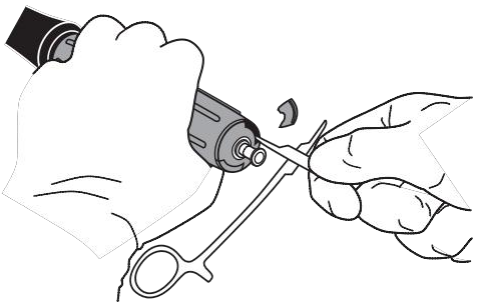
16



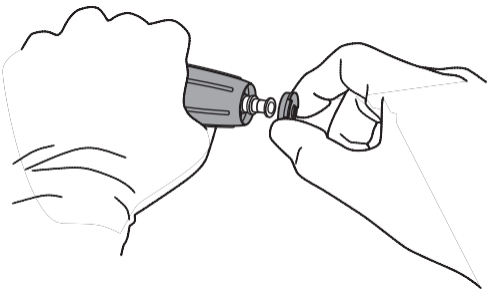
17



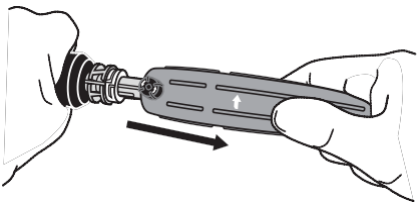
18



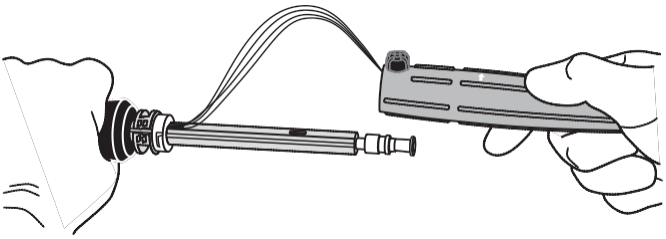
19



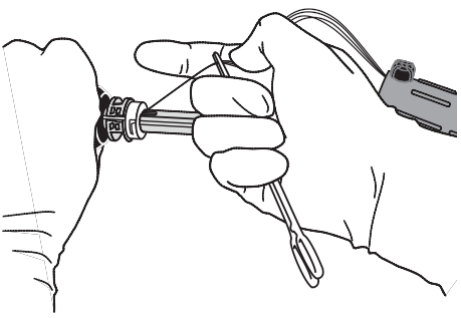
20



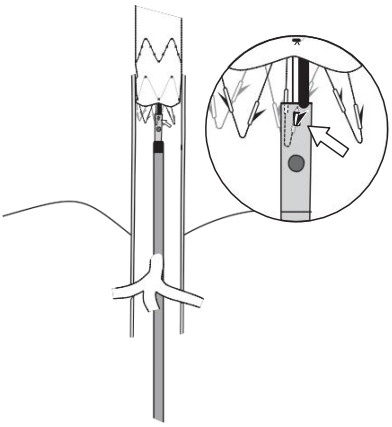
21



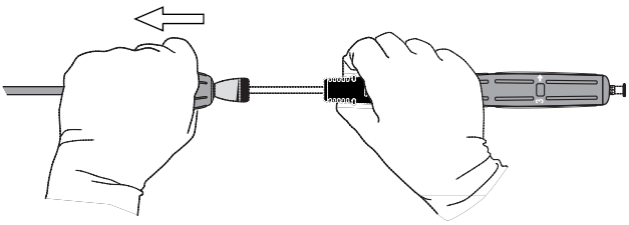
22



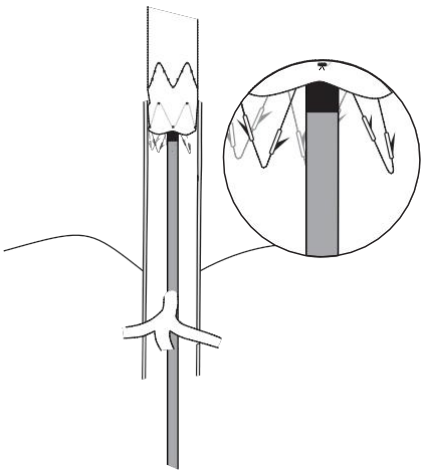
23



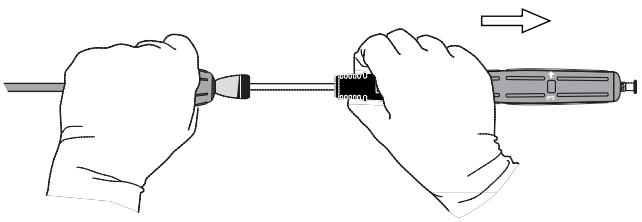
24



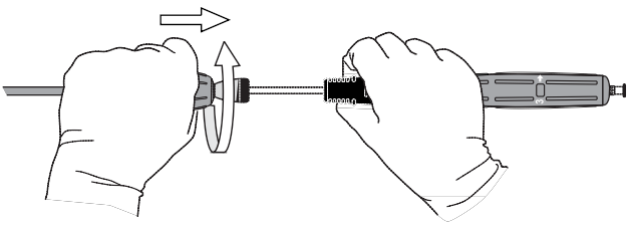
25



26



27



28

ZENITH ALPHA™ THORACIC ENDOVASCULAR GRAFT

Read all instructions carefully. Failure to properly follow the instructions, warnings, and precautions may lead to serious consequences or injury to the patient.

CAUTION: U.S. federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

CAUTION: All contents of the inner pouch (including the introduction system and endovascular graft) are supplied sterile, for single use only.

1 DEVICE DESCRIPTION

1.1 Zenith Alpha Thoracic Endovascular Graft

The Zenith Alpha Thoracic Endovascular Graft is a two-piece cylindrical endovascular graft consisting of proximal and distal components. The proximal component can be either tapered or nontapered and may be used independently (for ulcers/saccular aneurysms or blunt thoracic aortic injuries) or in combination with a distal component. The stent grafts are constructed of woven polyester fabric sewn to self-expanding nitinol stents with braided polyester and monofilament polypropylene suture. **(Fig. 1)** Both components are fully stented to provide stability and the expansile force necessary to open the lumen of the graft during deployment. Additionally, the nitinol stents provide the necessary attachment and seal of the graft to the vessel wall.

To assist with alignment, the proximal component has an uncovered stent. For added fixation and sealing, the proximal component has an internal sealing stent with fixation barbs that protrude through the graft material. In addition, the bare stent at the distal end of the distal component also contains barbs. On devices with diameters of 40-46 mm, the proximal sealing stent remains constrained to ensure alignment with the inner curvature of the aorta.

To facilitate fluoroscopic visualization of the stent graft, gold radiopaque markers are positioned on each end of the proximal and distal components. Gold markers are placed on stent apices at the proximal and distal aspects of the graft margins, denoting the edge of the graft material, to assist with deployment accuracy.

1.2 Introduction System

The Zenith Alpha Thoracic Endovascular Graft is shipped preloaded onto an introduction system. It has a sequential deployment method with built-in features to provide continuous control of the endovascular graft throughout the deployment procedure. The introduction system enables precise positioning before deployment of the proximal and distal components.

The main body graft components are deployed from a 16 French (6 mm OD), 18 French (7.1 mm OD), or 20 French (7.7 mm OD) introduction system. The proximal component's introduction system is slightly precurved to assist in proximal inferior wall apposition of the graft during deployment. (**Fig. 2**) These systems use either a single locking mechanism (for the proximal component and distal extension) or dual locking mechanisms (for the distal component) to secure the endovascular graft onto the introduction system until the physician releases it. All introduction systems are compatible with a .035 inch wire guide.

The introduction system features a Flexor® introducer sheath with a Captor Hemostatic Valve. For added hemostasis, the Captor Hemostatic Valve can be loosened or tightened for the introduction and/or removal of ancillary devices into and out of the sheath. The Flexor introducer sheath resists kinking and is hydrophilically coated. Both features are intended to enhance trackability in the iliac arteries and thoracic aorta.

1.3 Zenith Alpha Thoracic Endovascular Graft Ancillary Component

An endovascular ancillary component is available. The Zenith Alpha Thoracic Endovascular Graft ancillary component is a cylindrical component constructed from the same woven polyester fabric, self-expanding nitinol stents, and polyester and polypropylene suture used in the main body graft components. At the distal and proximal graft margins, the z-stents are attached to the inner surface for enhanced sealing. (**Fig. 1**) The ancillary component can be used to provide additional length to the endovascular graft distally or to increase the length of overlap between components. Additionally, the proximal component may be used to extend graft coverage proximally.

The Zenith Alpha Thoracic Endovascular Graft Distal Extension is deployed from a 16 French (6 mm OD), 18 French (7.1 mm OD), or 20 French (7.7 mm OD) introduction system. (**Fig. 2**) A single locking mechanism secures the endovascular graft to the introduction system until it is released by the physician. The locking mechanism is released by turning the rotation handle. All systems are compatible with a .035 inch wire guide.

To facilitate fluoroscopic visualization of the distal extension, gold radiopaque markers are positioned on the ends of the graft. Gold markers are placed on stent apices at the proximal and distal aspects of the graft margins, denoting the edge of the graft material, to assist with deployment accuracy.

2 INDICATIONS FOR USE

The Zenith Alpha Thoracic Endovascular Graft is indicated for the endovascular treatment of patients with isolated lesions of the descending thoracic aorta (not including dissections) having vascular anatomy suitable for endovascular repair, (**Fig. 3** and **Fig. 4**), including:

- Iliac/femoral anatomy that is suitable for access with the required introduction systems,
- Nonaneurysmal aortic segments (fixation sites) proximal and distal to the thoracic lesion:
  - with a length of at least 20 mm, and
  - with a diameter measured outer-wall-to-outer-wall of no greater than 42 mm and no less than 15 mm.

3 CONTRAINDICATIONS

The Zenith Alpha Thoracic Endovascular Graft is contraindicated in:

- Patients with known sensitivities or allergies to polyester, polypropylene, nitinol, or gold.
- Patients who have a condition that threatens to infect the endovascular graft.

4 WARNINGS AND PRECAUTIONS

4.1 General

- Read all instructions carefully. Failure to properly follow the instructions, warnings, and precautions may lead to serious consequences or injury to the patient.
- The Zenith Alpha Thoracic Endovascular Graft should be used only by physicians and teams trained in vascular interventional techniques (catheter based and surgical) and in the use of this device. Specific training expectations are described in **Section 10.1, Physician Training.**
- Additional endovascular interventions or conversion to standard open surgical repair following initial endovascular repair should be considered for patients experiencing enlarging aneurysms or ulcers, unacceptable decrease in fixation length (vessel and component overlap) and/or endoleak. An increase in aneurysm or ulcer size and/or persistent endoleak or migration may lead to rupture of the aneurysm or ulcer.
- Patients experiencing leaks or reduced blood flow through the graft may be required to undergo secondary endovascular interventions or surgical procedures.
- Always have a qualified surgery team available during implantation or reintervention procedures in the event that conversion to open surgical repair is necessary.

4.2 Patient Selection, Treatment and Follow-Up

- The Zenith Alpha Thoracic Endovascular Graft is designed to treat aortic neck diameters no smaller than 15 mm and no larger than 42 mm. The Zenith Alpha Thoracic Endovascular Graft is designed to treat proximal aortic necks (distal to either the left subclavian or left common carotid artery) of at least 20 mm in length. Additional proximal aortic neck length may be gained by covering the left subclavian artery (with or without discretionary transposition) when necessary to optimize device fixation and maximize aortic neck length. Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends. A distal aortic neck length of at least 20 mm proximal to the celiac axis is required. These sizing measurements are critical to the performance of the endovascular repair. In patients with large proximal aortic vessel diameter and aneurysms on the inner curvature, there is a risk that the graft may deploy in an angulated position if the sealing zone is less than 20 mm.
- Adequate iliac or femoral access is required to introduce the device into the vasculature. Careful evaluation of vessel size, anatomy, and disease state is required to ensure successful sheath introduction and subsequent withdrawal, as vessels that are significantly calcified, occlusive, tortuous, or thrombus lined may preclude introduction of the endovascular graft and/or increase the risk of embolization. A vascular conduit technique may be necessary to achieve access in some patients.
- Key anatomic elements that may affect successful exclusion of the thoracic lesion include severe angulation (radius of curvature < 20 mm and localized angulation > 45 degrees); short proximal or distal fixation sites (< 20 mm); an inverted funnel shape at the proximal fixation site or a funnel shape at the distal fixation site (greater than a 10% change in diameter over 20 mm of fixation site length); and circumferential thrombus and/or calcification at the arterial fixation sites. Irregular calcification and/or plaque may compromise the attachment and sealing at the fixation sites. In the presence of anatomical limitations, a longer neck length may be required to obtain adequate sealing and fixation. Necks exhibiting these key anatomic elements may be more conducive to graft migration. In patients with large aneurysms on the outer curvature close to the left subclavian, it may be difficult to track the device around the arch, and extra support may be needed using a brachio-femoral wire. If difficulty is noted in tracking the second component through tortuous anatomy of the thoracic aorta, extra support may be provided using a brachio-femoral wire.
- The safety and effectiveness of the Zenith Alpha Thoracic Endovascular Graft and ancillary components have not been evaluated in the following patient populations:
  - aortobronchial and aortoesophageal fistulas
  - aortitis or inflammatory aneurysms
  - diagnosed or suspected genetic connective tissue disease (e.g., Marfans or Ehlers-Danlos Syndrome)
  - dissections
  - females who are pregnant, breastfeeding, or planning to become pregnant within 60 months
  - leaking, pending rupture or ruptured aneurysm
  - patients less than 18 years of age
  - mycotic aneurysms
  - pseudoaneurysms resulting from previous graft placement
  - systemic infection (e.g., sepsis)
  - access vessels that preclude safe insertion
  - inability to preserve the left common carotid artery and celiac artery
  - previous repair in descending thoracic aorta
  - surgical or endovascular AAA repair within 30 days before or after TAA repair
  - bleeding diathesis, uncorrectable coagulopathy, or refuses blood transfusion
  - stroke within 3 months
  - untreatable reaction to contrast, which cannot be adequately premedicated
- Successful patient selection requires specific imaging and accurate measurements; please see **Section 4.3, Pre-Procedure Measurement Techniques and Imaging.**
- If occlusion of the left subclavian artery ostium is required to obtain adequate neck length for fixation and sealing, transposition or bypass of the left subclavian artery may be warranted.
- The Zenith Alpha Thoracic Endovascular Graft is not recommended for patients who cannot tolerate contrast agents necessary for intraoperative and postoperative follow-up imaging, or who are unable to undergo, or will not be compliant with the necessary preoperative and postoperative imaging and implantation studies as described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP**. All patients should be monitored closely and checked periodically for change in the condition of their disease and the integrity of the endoprosthesis.
- The Zenith Alpha Thoracic Endovascular Graft is not recommended for patients whose weight and/or size would compromise or prevent the necessary imaging requirements.
- Graft implantation may increase the risk of paraplegia or paraparesis where graft exclusion covers the origins of dominant spinal cord or intercostal arteries.
  - **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the endovascular graft) should receive enhanced follow-up. Specific follow-up guidelines are described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP.**
  - The long-term performance of endovascular grafts has not yet been established in young patients and patients performing extreme sports.
  - After endovascular graft placement, patients should be regularly monitored for endoleak flow, thoracic lesion growth, or changes in the structure or position of the endovascular graft.

4.3 Pre-Procedure Measurement Techniques and Imaging

- All lengths and diameters of the devices necessary to complete the procedure should be available to the physician, especially when pre-operative case planning measurements (treatment diameters/lengths) are not certain. This approach allows for greater intra-operative flexibility to achieve optimal procedural outcomes.
- Lack of non-contrast CT imaging may result in failure to appreciate iliac or aortic calcification that may preclude access or reliable device fixation and seal.
- Pre-procedure imaging reconstruction thicknesses > 3 mm may result in suboptimal device sizing, or in failure to appreciate focal stenoses from CT.
- Clinical experience indicates that contrast-enhanced spiral computed tomographic angiography (CTA) with 3-D reconstruction is the strongly recommended imaging modality to accurately assess patient anatomy prior to treatment with the Zenith Alpha Thoracic Endovascular Graft. If contrast-enhanced spiral CTA with 3-D reconstruction is not available, the patient should be referred to a facility with these capabilities.
- Clinicians recommend positioning the x-ray C-arm during procedural angiography so that it is perpendicular to the aortic vessel neck proximal to the thoracic lesion, typically 45-75 degrees left anterior oblique (LAO) for the arch.

- **Diameter:** A contrast-enhanced spiral CTA is strongly recommended for measuring aortic diameter. Diameter measurements should be determined from the outer-wall-to-outer-wall vessel diameter and not the lumen diameter. The spiral CTA scan must include the great vessels through the femoral heads at an axial slice thickness of 3 mm or less. **For blunt thoracic aortic injury patients, CTA measurements should be based on a CTA of a fully resuscitated patient**.
- Clinical experience has shown that temporary changes in aortic diameter during blood loss can lead to incorrect aortic measurement on preoperative CTA, inadequate sizing, and increased risks of graft complications, migration and endoleak, as observed during the clinical study. If preoperative CTA is done during hemodynamic instability, repeat CTA when the patient is stable or use IVUS at the time of the procedure to confirm diameter measurements. For patients with blunt thoracic aortic injuries, if there is significant periaortic hematoma in the region of the subclavian artery the hematoma should not be counted in the diameter measurement, as there is a risk of oversizing the graft.
- **Length:** Clinical experience indicates that 3-D CTA reconstruction is the strongly recommended imaging modality to accurately assess proximal and distal neck lengths for the Zenith Alpha Thoracic Endovascular Graft. These reconstructions should be performed in sagittal, coronal, and varying oblique views depending upon individual patient anatomy. If 3-D reconstruction is not available, the patient should be referred to a facility with these capabilities. **Length measurements should be taken along the greater curvature of the aorta, including the aneurysm, if present.**

  NOTE: The greater curvature is the longest measurement following the curve of the aneurysm and may be on the outer or inner curvature of the aorta depending on the location of the aneurysm.

  NOTE: Large aneurysms and difficult anatomy may require extra care in planning.

4.4 Device Selection

- **Strict adherence to the Zenith Alpha Thoracic Endovascular Graft IFU sizing guide both in terms of component diameter (Tables 1 and 2 in Section 10.5 Device Diameter Sizing Guidelines) as well as component type/length (as stated below and in Section 10.6 Device Length Sizing Guidelines) is strongly recommended in order to mitigate the risk for events (e.g., migration, endoleak, aneurysm growth) that could result from selecting inappropriate device sizes**.
- **Tables 1** and **2** incorporate appropriate device oversizing. Sizing outside of the recommendations provided in Tables 1 and 2, including that which could result from a difference in location of graft deployment relative to the location used for graft sizing, can result in aneurysm growth, endoleak, and migration, as observed in the clinical studies (refer to the Device Performance sections in the SUMMARY OF CLINICAL DATA). Fracture, device infolding, or compression may also result.
- Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends.
- To treat more focal aortic injuries, as often found in blunt thoracic aortic injury patients, a proximal component can be used alone.
- In aneurysms the graft may settle into the greater curve of the aneurysm over time. Accordingly, extra graft length needs to be planned.
  - A two-component repair (proximal and distal component) is recommended, as it provides the ability to adapt to the length change over time. A two-component repair (proximal and distal component) also provides active fixation at both the proximal and distal seal sites.
  - The minimum required amount of overlap between devices is three stents. Less than a three-stent overlap may result in endoleak (with or without component separation). However, no part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall. Device lengths should be selected accordingly.
  - If an acceptable two-component (proximal and distal component) treatment plan cannot be achieved (e.g., excessive aortic coverage, even with maximal overlap of shortest components), the proximal component must be selected with enough length to achieve and maintain the minimum 20 mm sealing zones at both ends even when positioned in the greater curve of the aneurysm. Failure to do so could result in migration, endoleak, and aneurysm growth, as observed in the clinical study (refer to the Device Performance section in the SUMMARY OF CLINICAL DATA from the aneurysm/ulcer study).

4.5 Implant Procedure

- Systemic anticoagulation should be used during the implantation procedure based on hospital- and physician-preferred protocol. If heparin is contraindicated, an alternative anticoagulant should be used.
- Appropriate procedural imaging is required to successfully position the Zenith Alpha Thoracic Endovascular Graft and ensure accurate apposition to the aortic wall.
- Fluoroscopy should be used during introduction and deployment to confirm proper operation of the introduction system components, proper placement of the graft, and desired procedural outcome.
- The use of the Zenith Alpha Thoracic Endovascular Graft requires administration of intravascular contrast. Patients with pre-existing renal insufficiency may have an increased risk of renal failure postoperatively. Care should be taken to limit the amount of contrast media used during the procedure, and to observe preventative methods of treatment to decrease renal compromise (e.g., adequate hydration).
- Use caution during manipulation of catheters, wires, and sheaths within the thoracic lesion. Significant disturbances may dislodge fragments of thrombus or plaque, which can cause distal or cerebral embolization, or cause rupture of the thoracic lesion or aorta.
- Minimize handling of the constrained endoprosthesis during preparation and insertion to decrease the risk of endoprosthesis contamination and infection.
- To activate the hydrophilic coating on the outside of the Flexor introducer sheath, the surface must be wiped with sterile gauze pads soaked in saline solution. Always keep the sheath hydrated for optimal performance.
- Maintain wire guide position during introduction system insertion.
- Do not bend or kink the introduction system. Doing so may cause damage to the introduction system and the Zenith Alpha Thoracic Endovascular Graft.
- To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.
- To avoid damage to the sheath, be careful to advance all components of the system together (from outer sheath to inner cannula).
- Do not continue advancing the wire guide or any portion of the introduction system if resistance is felt. Stop and assess the cause of resistance; vessel, catheter, or graft damage may occur. Exercise particular care in areas of stenosis, intravascular thrombosis, or calcified or tortuous vessels.
- As the sheath and/or wire guide is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check the position as necessary.
- During sheath withdrawal, the uncovered proximal stent and covered proximal stent with barbs are in contact with the vessel wall. At this stage it may be possible to advance the device, but retraction may cause aortic wall damage.
- Inaccurate placement and/or incomplete sealing of the Zenith Alpha Thoracic Endovascular Graft within the vessel may result in increased risk of endoleak, migration, or inadvertent occlusion of the left subclavian, left common carotid, and/or celiac arteries.
- Inadequate fixation of the Zenith Alpha Thoracic Endovascular Graft may result in increased risk of migration of the stent graft. Incorrect deployment or migration of the stent graft may require surgical intervention.
- Inadvertent partial deployment or migration of the endoprosthesis may require surgical removal.
- Land the proximal and the distal ends of the device in parallel aortic neck segments without acute angulation (> 45 degrees) or circumferential thrombus/calcification to ensure fixation and seal.
- Be sure to land the proximal and distal ends of the device in an aortic neck segment with a diameter that matches the initial sizing of the device. Landing in a segment that is < 10% or > 25% of the diameter to which the device was sized may potentially result in inadequate sizing and therefore migration, endoleak, thoracic lesion growth, or increased risk of thrombosis.
- The Zenith Alpha Thoracic Endovascular Graft incorporates an uncovered proximal stent, a covered proximal stent (on the proximal component) with fixation barbs, and an uncovered distal stent (on the distal component) with fixation barbs. Exercise extreme caution when manipulating interventional and angiographic devices in the region of the uncovered proximal stent and uncovered distal stent.
- When using a distal component, take care to avoid landing the distal bare stent in tortuous anatomy (i.e., localized angulation > 45 degrees).
- Unless medically indicated, do not deploy the Zenith Alpha Thoracic Endovascular Graft in a location that will occlude arteries necessary to supply blood flow to organs or extremities. Do not cover significant arch or mesenteric arteries (exception may be the left subclavian artery) with the device. Vessel occlusion may occur. If a left subclavian artery is to be covered with the device, the clinician should be aware of the possibility of compromise to cerebral and upper limb circulation and collateral circulation to the spinal cord.
- Take care not to advance the sheath while the stent graft is still within it. Advancing the sheath at this stage may cause the barbs to perforate the introducer sheath.
- Do not attempt to resheath the graft after partial or complete deployment.
- Repositioning the stent graft distally after partial deployment of the covered proximal stent may result in damage to the stent graft and/or vessel injury.
- To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.
- In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers demonstrate that there is adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.

  NOTE: If endoleaks or other problems are observed, (e.g., inadequate seal length or overlap length) refer to **Section 11.2, Ancillary Devices: Distal Extensions**.
- In the event that reinstrumentation (secondary intervention) of the graft is necessary, avoid damaging the graft or disturbing the graft's position.

4.6 Molding Balloon Use – Optional

- Do not inflate the balloon in the aorta outside of the graft, as doing so may cause damage to the aorta. Use the molding balloon in accordance with its labeling.
- Use care when inflating the balloon within the graft in the presence of calcification, as excessive inflation may cause damage to the aorta.
- Confirm complete deflation of the balloon prior to repositioning.
- For added hemostasis, the Captor Hemostatic Valve can be loosened or tightened to accommodate the insertion and subsequent withdrawal of a molding balloon.

4.7 MRI Safety Information

Nonclinical testing has demonstrated that the Zenith Alpha Thoracic Endovascular Graft is MR Conditional according to ASTM F2503. A patient with this endovascular graft can be scanned safely in a 1.5 T or 3.0 T MR system using the specific testing parameters described in Section 12.4. Additional MRI safety information is found in Section 12.4.

5 POTENTIAL ADVERSE EVENTS

Adverse events associated with either the Zenith Alpha Thoracic Endovascular Graft or the implantation procedure that may occur and/or require intervention include, but are not limited to:

- Amputation
- Anesthetic complications and subsequent attendant problems (e.g., aspiration)
- Aneurysm enlargement
- Aneurysm rupture and death
- Aortic damage, including perforation, dissection, bleeding, rupture and death
- Aortic valve damage
- Aorto-bronchial fistula
- Aorto-esophageal fistula
- Arterial or venous thrombosis and/or pseudoaneurysm
- Arteriovenous fistula
- Bleeding, hematoma, or coagulopathy
- Bowel complications (e.g., ileus, transient ischemia, infarction, necrosis)
- Cardiac complications and subsequent attendant problems (e.g., arrhythmia, tamponade, myocardial infarction, congestive heart failure, hypotension, hypertension)
- Claudication (e.g., buttock, lower limb)
- Death
- Edema
- Embolization (micro and macro) with transient or permanent ischemia or infarction
- Endoleak
- Endovascular graft: improper component placement, incomplete component deployment, component migration and/or separation, suture break, occlusion, infection, stent fracture, stent corrosion, graft material wear, dilatation, erosion, puncture, perigraft flow, barb separation
- Femoral neuropathy
- Fever and localized inflammation
- Genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, fistula, urinary incontinence, hematuria, infection)
- Hepatic failure
- Impotence
- Infection of the aneurysm, device or access site, including abscess formation, transient fever and pain
- Lymphatic complications and subsequent attendant problems (e.g., lymph fistula, lymphocele)
- Local or systemic neurologic complications and subsequent attendant problems (e.g., stroke, transient ischemic attack, paraplegia, paraparesis, spinal cord shock, paralysis)
- Occlusion of coronary arteries
- Pulmonary embolism
- Pulmonary/respiratory complications and subsequent attendant problems (e.g., pneumonia, respiratory failure, prolonged intubation)
- Renal complications and subsequent attendant problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- Surgical conversion to open repair
- Vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula
- Vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death)
- Vessel damage
- Wound complications and subsequent problems (e.g., dehiscence, infection)

DEVICE RELATED ADVERSE EVENT REPORTING

Any adverse event (clinical incident) involving the Zenith Alpha Thoracic Endovascular Graft should be reported to COOK immediately. To report an incident, call the Customer Relations Department at 1-800-457-4500 (24 hour) or 1-812-339-2235.

6 SUMMARY OF CLINICAL DATA

A summary of the clinical data can be found on **www.cookmedical.com.**

7 PATIENT SELECTION AND TREATMENT

(See **Section 4, WARNINGS AND PRECAUTIONS**)

7.1 Individualization of Treatment

Cook recommends that the Zenith Alpha Thoracic Endovascular Graft component diameters be selected as described in **Tables 1** and **2**. All lengths and diameters of the devices necessary to complete the procedure should be available to the physician, especially when preoperative case planning measurements (treatment diameters and lengths) are not certain. This approach allows for greater intraoperative flexibility.

The risks and benefits should be carefully considered for each patient before use of the Zenith Alpha Thoracic Endovascular Graft. Additional considerations for patient selection include, but are not limited to:

- Patient's age and life expectancy
- Comorbidities (e.g., cardiac, pulmonary, or renal insufficiency prior to surgery, morbid obesity)
- Patient's suitability for open surgical repair
- The risk of thoracic lesion rupture compared to the risk of treatment with the Zenith Alpha Thoracic Endovascular Graft
- Ability to tolerate general, regional, or local anesthesia
- Ability and willingness to undergo and comply with the required follow-up
- Iliofemoral access vessel size and morphology (thrombus, calcification and/or tortuosity) should be compatible with vascular access techniques and accessories of the delivery profile of a 16 French (6 mm OD) to 20 French (7.7 mm OD) vascular introducer sheath
- Vascular morphology suitable for endovascular repair, including:
  - Radius of curvature greater than or equal to 20 mm along the entire length of aorta intended to be treated.
- Nonaneurysmal aortic segments (fixation sites) proximal and distal to the thoracic lesion:
  - with a length of at least 20 mm,
  - with a diameter measured outer-wall-to-outer-wall of no greater than 42 mm and no less than 15 mm, and with localized angulations less than 45 degrees.

The final treatment decision is at the discretion of the physician and patient.

8 PATIENT COUNSELING INFORMATION

The physician and patient (and/or family members) should review the risks and benefits when discussing this endovascular device and procedure, including:

- Risks and differences between endovascular repair and open surgical repair
- Potential advantages of traditional open surgical repair
- Potential advantages of endovascular repair
- The possibility that subsequent interventional or open surgical repair of the thoracic lesion may be required after initial endovascular repair.

In addition to the risks and benefits of an endovascular repair, the physician should assess the patient's commitment to and compliance with postoperative follow-up as necessary to ensure continuing safe and effective results. Listed below are additional topics to discuss with the patient as to expectations after an endovascular repair:

- **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcer, or changes in the structure or position of the endovascular graft) should receive enhanced follow-up. Specific follow-up guidelines are described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP.**
- Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be told that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of thoracic aortic lesions. At a minimum, annual imaging and adherence to routine postoperative follow-up requirements is required and should be considered a life-long commitment to the patient's health and well-being.
- The patient should be told that successful thoracic lesion repair does not arrest the disease process. It is still possible to have associated degeneration of vessels.
- Physicians must advise every patient that it is important to seek prompt medical attention if he/she experiences signs of graft occlusion, thoracic lesion enlargement or rupture. Signs of graft occlusion include, but may not be limited to, pulse-less legs, ischemia of intestines, and cold extremities. Thoracic lesion rupture may be asymptomatic, but usually presents as back or chest pain, persistent cough, dizziness, fainting, rapid heartbeat, or sudden weakness.
- Due to the imaging required for successful placement and follow-up of endovascular devices, the risk of radiation exposure to developing tissue should be discussed with women who are or suspect they are pregnant.
- Men who undergo endovascular or open surgical repair may experience impotence.

The physician should complete the Patient ID Card and give it to the patient so that he/she can carry it with him/her at all times. The patient should refer to the card any time he/she visits additional health practitioners, particularly for any additional diagnostic procedures (e.g., MRI).

9 HOW SUPPLIED

- The Zenith Alpha Thoracic Endovascular Graft is sterilized by ethylene oxide gas, is preloaded onto an introduction system, and is supplied in peel-open packages.
- The device is intended for single use only. Do not resterilize the device.
- The product is sterile if the package is unopened and undamaged. Inspect the device and packaging to verify that no damage has occurred as a result of shipping. Do not use this device if damage has occurred or if the sterilization barrier has been damaged or broken. If damage has occurred, do not use the product; instead, return the product to Cook.
- Prior to use, verify that the correct devices (quantity and size) have been supplied for the patient by matching the device to the order prescribed by the physician for that particular patient.
- The device is loaded into a 16 French, 18 French or 20 French Flexor Introducer Sheath. Its surface is treated with a hydrophilic coating that, when hydrated, enhances trackability. To activate the hydrophilic coating, the surface must be wiped with a sterile gauze pad soaked in saline solution under sterile conditions.
- Do not use after the expiration date printed on the label.
- Store in a dark, cool, dry place.

10 CLINICAL USE INFORMATION

10.1 Physician Training

CAUTION: Always have a qualified surgery team available during implantation or reintervention procedures in the event that conversion to open surgical repair is necessary.

CAUTION: The Zenith Alpha Thoracic Endovascular Graft should only be used by physicians and teams trained in vascular interventional techniques (endovascular and surgical) and in the use of this device. The recommended skill and knowledge requirements for physicians using the Zenith Alpha Thoracic Endovascular Graft are outlined below:

Patient Selection

- Knowledge of the natural history of thoracic aortic lesions (aneurysms, ulcers, or blunt thoracic aortic injury) and comorbidities associated with thoracic aortic lesion repair.
- Knowledge of radiographic image interpretation, patient selection, device selection, planning, and sizing.

A multidisciplinary team that has combined procedural experience with:

- Femoral and brachial cutdown, arteriotomy, and repair or conduit technique
- Percutaneous access and closure techniques
- Nonselective and selective wire guide and catheter techniques
- Fluoroscopic and angiographic image interpretation
- Embolization
- Angioplasty
- Endovascular stent placement
- Snare techniques
- Appropriate use of radiographic contrast material
- Techniques to minimize radiation exposure
- Expertise in necessary patient follow-up modalities

10.2 Inspection Prior to Use

Inspect the device and packaging to verify that no damage has occurred as a result of shipping. Do not use this device if damage has occurred or if the sterilization barrier has been damaged or broken. If damage has occurred, do not use the product; instead, return the product to Cook. Prior to use, verify correct devices (quantity and size) have been supplied for the patient by matching the device to the order prescribed by the physician for that particular patient.

10.3 Materials Required

(Not included in the endovascular graft system)

- A selection of Zenith Alpha Thoracic Endovascular Graft distal ancillary components in diameters compatible with the proximal and distal components.
- Fluoroscope with digital angiography capabilities (C-arm or fixed unit)
- Contrast media
- Power injector
- Syringe
- Heparinized saline solution
- Sterile gauze pads

10.4 Materials Recommended

The following products are recommended for implantation of any component in the Zenith product line. For information on the use of these products, refer to the individual product's **Suggested Instructions for Use**:

- .035 inch (0.89 mm) extra stiff wire guide, 260/300 cm:
  - Cook Lunderquist Extra Stiff Wire Guides (LESDC)
  - Cook Amplatz Ultra Stiff Wire Guides (AUS)
- .035 inch (0.89 mm) standard wire guide:
  - Cook .035 inch Wire Guides
  - Cook .035 inch Bentson Wire Guide
  - Cook Nimble® Wire Guides
- Molding balloons:
  - Cook Coda® Balloon Catheters
- Introducer sets:
  - Cook Check-Flo® Introducer Sets
- Sizing catheter:
  - Cook Aurous® Centimeter Sizing Catheters
- Angiographic radiopaque marker catheters:
  - Cook Beacon® Tip Angiographic Catheters
  - Cook Beacon® Tip Royal Flush Catheters, 125 cm
- Entry needles:
  - Cook single wall entry needles
- Endovascular dilators:
  - Cook endovascular dilator sets

10.5 Device Diameter Sizing Guidelines

The choice of diameter should be determined from the outer-wall-to-outer-wall vessel diameter and **not** the lumen diameter. Undersizing (as observed during the clinical studies; refer to the Device Performance sections in the SUMMARY OF CLINICAL DATA) or oversizing may result in incomplete sealing or compromised flow. In order to ensure accurate diameter measurements for the purpose of graft sizing, particularly when in curved segments of the aorta, measure the aortic diameter using 3D reconstructed views perpendicular to the aortic centerline of flow. The proximal diameter of the distal component can be up to 8 mm larger in diameter than the distal diameter of the proximal component. It is strongly recommended that you ensure a minimum three-stent overlap between components.

For patients with blunt thoracic aortic injuries, if there is significant periaortic hematoma in the region of the subclavian artery the hematoma should not be counted in the diameter measurement, as there is a risk of oversizing the graft. For blunt thoracic aortic injury patients, CTA measurements should be based on a CTA of a fully resuscitated patient.

Table 1 – Proximal, Distal and Proximal Tapered Component (P, D, PT) Graft Diameter Sizing Guide*

Intended Aortic Vessel Diameter[1,2] (mm)	Graft Diameter[3] (mm)	Overall Length of Proximal Component (mm)	Overall Length of Distal Component (mm)	Overall Length of Tapered Proximal Component (mm)	Introducer Sheath (Fr)	Introducer Sheath Outer Diameter (OD) (mm)
15	18	105/127**	n/a	n/a	16	6.0
16	18	105/127**	n/a	n/a	16	6.0
17	20	105/127**	n/a	n/a	16	6.0
18	22	105/127**	n/a	105**	16	6.0
19	22	105/127**	n/a	105**	16	6.0
20	24	105/127**	n/a	n/a	16	6.0
21	24	105/127**	n/a	n/a	16	6.0
22	26	105/149**	n/a	105	16	6.0
23	26	105/149**	n/a	105	16	6.0
24	28	109/132**/155/201	160/229**	n/a	16	6.0
25	28	109/132**/155/201	160/229**	n/a	16	6.0
26	30	109/132**/155/201	160/229**	108	16	6.0
27	30	109/132**/155/201	160/229**	108	16	6.0
28	32	109/132**/155/201	160/229**	178/201	18	7.1
29	32	109/132**/155/201	160/229**	178/201	18	7.1
30	34	113/137**/161/209	142/190	161/209	18	7.1
31	36	113/137**/161/209	142/190	161/209	18	7.1
32	36	113/137**/161/209	142/190	161/209	18	7.1
33	38	117/142**/167/217	147/197	167/217	18	7.1
34	38	117/142**/167/217	147/197	167/217	18	7.1
35	40	117/142**/167/217	147/197	167/217	20	7.7
36	40	117/142**/167/217	147/197	167/217	20	7.7
37	42	121/147**/173/225	152**/204	173/225	20	7.7
38	42	121/147**/173/225	152**/204	173/225	20	7.7
39	44	125/152**/179/233	157**/211	179/233	20	7.7
40	46	125/152**/179/233	157**/211	179/233	20	7.7
41	46	125/152**/179/233	157**/211	179/233	20	7.7
42	46	125/152**/179/233	157**/211	179/233	20	7.7

*All dimensions are nominal.

**Non stock items.

[1] Maximum diameter along the fixation site, measured outer-wall-to-outer-wall.

[2] Round the measured aortic diameter to the nearest mm.

[3] Additional considerations may affect the choice of diameter.

Table 2 – Distal Extension (DE) Graft Diameter Sizing Guide*

Intended Aortic Vessel Diameter[1,2] (mm)	Graft Diameter[3] (mm)
15	18
16	18
17	20
18	22
19	22
20	24
21	24
22	26
23	26
24	28
25	28
26	30
27	30
28	32
29	32
30	34
31	36
32	36
33	38
34	38
35	40
36	40
37	42
38	42
39	44
40	46
41	46
42	46

*All dimensions are nominal.
**Non stock items.
[1] Maximum diameter along the fixation site, measured outer-wall-to-outer-wall.
[2] Round the measured aortic diameter to the nearest mm.
[3] Additional considerations may affect the choice of diameter.

10.6 Device Length Sizing Guidelines

- Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends.
- To treat more focal aortic injuries, as often found in blunt thoracic aortic injury patients, a proximal component can be used alone.
- In aneurysms the graft may settle into the greater curve of the aneurysm over time. Accordingly, extra graft length needs to be planned.
  - A two-component repair (proximal and distal component) is recommended, as it provides the ability to adapt to the length change over time. A two-component repair (proximal and distal component) also provides active fixation at both the proximal and distal seal sites.
  - The minimum required amount of overlap between devices is three stents. Less than a three-stent overlap may result in endoleak (with or without component separation). However, no part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall. Device lengths should be selected accordingly.
  - If an acceptable two-component (proximal and distal component) treatment plan cannot be achieved (e.g., excessive aortic coverage, even with maximal overlap of shortest components), the proximal component must be selected with enough length to achieve and maintain the minimum 20 mm sealing zones at both ends even when positioned in the greater curve of the aneurysm. Failure to do so could result in migration, endoleak, and aneurysm growth, as observed in the clinical study (refer to the Device Performance section in the SUMMARY OF CLINICAL DATA from the aneurysm/ulcer study).

11 DIRECTIONS FOR USE

Anatomical Requirements

- Iliofemoral access vessel size and morphology (minimal thrombus, calcium and/or tortuosity) should be compatible with vascular access techniques and accessories. Arterial conduit technique may be required.
- Proximal and distal aortic neck lengths should be a minimum of 20 mm.
- Aortic neck diameters measured outer-wall-to-outer-wall should be between 15-42 mm.
- A proximal neck diameter that is 4 mm or more larger than the distal neck diameter requires the use of a proximal tapered component.
- No localized angulation should be larger than 45 degrees.
- Measurements to be taken during the pretreatment assessment are shown in **Fig. 3** and **Fig. 4.**

Proximal and Distal Component Overlap

A minimum overlap of three stents is recommended; however, the proximal sealing stent of the proximal component or distal sealing stent of the distal component should not be overlapped.

Prior to use of the Zenith Alpha Thoracic Endovascular Graft, review the Suggested Instructions for Use booklet. The following instructions are intended to help guide the physician and do not take the place of physician judgment.

General Use Information

Standard techniques for placement of arterial access sheaths, guiding catheters, angiographic catheters, and wire guides should be employed during use of the Zenith Alpha Thoracic Endovascular Graft. The Zenith Alpha Thoracic Endovascular Graft is compatible with .035 inch diameter wire guides. Brachio-femoral wire guide technique may be required if the patient has a difficult anatomy.

Endovascular stenting is a surgical procedure, and blood loss from various causes may occur, infrequently requiring intervention (including transfusion) to prevent adverse outcomes. It is important to monitor blood loss from the hemostatic valve throughout the procedure, but is specifically relevant during and after manipulation of the gray positioner. After the gray positioner has been removed, if blood loss is excessive, consider placing an uninflated molding balloon or an introduction system dilator within the valve to restrict flow.

Pre-Implant Determinants

Verify from pre-implant planning that the correct device has been selected. Determinants include:

- Femoral artery selection for introduction of the introduction system(s)
- Angulation of aorta, aneurysm, and iliac arteries
- Quality of the proximal and distal fixation sites
- Diameters of proximal and distal fixation sites and distal iliac arteries
- Length of proximal and distal fixation sites

Patient Preparation

1. Refer to institutional protocols relating to anesthesia, anticoagulation, and monitoring of vital signs.
2. Position the patient on the imaging table to allow fluoroscopic visualization from the aortic arch to the femoral bifurcations.
3. Expose the femoral artery using standard surgical technique.
4. Establish adequate proximal and distal vascular control of the femoral artery.

11.1 The Zenith Alpha Thoracic Endovascular Graft

11.1.1 Proximal and Distal Components Preparation/Flush

1. Remove the yellow-hubbed inner stylet from the dilator tip. Verify that the Captor Sleeve is within the Captor Hemostatic Valve; do not remove the Captor Sleeve. (**Fig. 5**)
2. Elevate the distal tip of the system and flush through the hemostatic valve until fluid exits the tip of the introducer sheath. (**Fig. 6**) Continue to inject a further 10 ml of flushing solution through the device. Discontinue injection and close the stopcock on the connecting tube.
   NOTE: Graft flushing solution of heparinized saline is often used.
3. Attach a syringe with heparinized saline to the hub on the rotation handle. (**Fig. 7**) Flush until fluid exits the distal sideports and dilator tip.
4. Soak sterile gauze pads in saline solution and use them to wipe the Flexor Introducer Sheath to activate the hydrophilic coating. Hydrate both sheath and dilator tip liberally.

11.1.2 Placement of Proximal Component

1. Puncture the selected artery using standard technique with an 18-gage access needle. Upon vessel entry, insert:
   - Wire guide – standard .035 inch, 260/300 cm, 15 mm J tip or Benson wire guide.
   - Appropriate size sheath (e.g., 5 French).
   - Pigtail flush catheter (often radiopaque-banded sizing catheters; e.g., Cook Centimeter Sizing CSC-20 catheter).
2. Perform angiography at the appropriate level. If using radiopaque markers, adjust position of the catheter as necessary and repeat angiography.
3. Ensure the graft system has been flushed and primed with heparinized saline (appropriate flush solution), and all air has been removed.
4. Give systemic heparin. Flush all catheters and wet all wire guides with heparinized saline. Reflush catheters and rewet wire guides after each exchange.
5. Replace the standard wire guide with a stiff .035 inch, 260/300 cm, LESDC wire guide and advance through the catheter and up to the aortic arch.
   NOTE: If the anatomy is difficult, consider using a brachio-femoral approach instead.
6. Remove the pigtail flush catheter and sheath.
   NOTE: At this stage, the second femoral artery can be accessed for angiographic catheter placement. Alternatively, consider using a brachial approach.
7. Introduce the freshly hydrated introduction system over the wire guide and advance it until the desired graft position is reached.
   CAUTION: To avoid inadvertent displacement of the graft during withdrawal of the sheath, it may be appropriate to momentarily decrease the patient's mean arterial pressure to approximately 80 mm Hg (at the discretion of the physician).
   CAUTION: To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.
   NOTE: The dilator tip will soften at body temperature.
8. Verify wire guide position in the aortic arch. Ensure correct graft position.
   CAUTION: Care should be taken not to advance the sheath while the stent graft is still within it. Advancing the sheath at this stage may cause the barbs to perforate the introducer sheath.
9. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned to the open position. (**Fig. 8**)
10. Stabilize the gray positioner (introduction system shaft) and withdraw the sheath until the graft is fully expanded and the valve assembly with the Captor Sleeve docks with the black gripper. (**Fig. 9**)
    CAUTION: As the sheath is withdrawn, anatomy and graft position may change. Prior to complete unsheathing of the graft, check distal gold markers to make sure visceral arteries will not be covered. Constantly monitor graft position and perform angiography to check position as necessary.
    CAUTION: During sheath withdrawal, the proximal barbs are exposed and are in contact with the vessel wall. At this stage it may be possible to advance the device, but retraction may cause aortic wall damage.
    NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.
11. Verify graft position and, if necessary, adjust it forward. Recheck graft position with angiography.
    NOTE: If an angiographic catheter is placed parallel to the stent graft, use this to perform position angiography.
12. While holding the black gripper, turn the black safety-lock knob in the direction of the arrows to engage the blue rotation handle. (**Fig. 10**) Make sure the black safety-lock knob is in the unlocked position.
13. Under fluoroscopy, turn the blue rotation handle in the direction of the arrow until a stop is felt. (**Fig. 11**) This indicates that the uncovered stent and proximal end of the graft have opened and that the distal attachment to the introducer has been released.
    NOTE: If the blue rotation handle stops before completing the rotation (so that the proximal end of the graft is not released from the introduction system), verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.
    NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation

handle will remain engaged. Continue with the procedure.

NOTE: If it is still difficult to rotate the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

14. Remove the introduction system, leaving the wire guide in the graft.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

NOTE: Inaccuracies in device size selection or placement, changes or anomalies in patient anatomy, or procedural complications may require placement of additional endovascular grafts and extensions to achieve the minimum length of proximal and distal seal and length of overlap between components.

11.1.3 Placement of Distal Component

1. If an angiographic catheter is placed in the femoral artery, it should be repositioned to demonstrate the aortic anatomy where the distal component is to be deployed.
2. Introduce the freshly hydrated introduction system over the wire guide until the desired graft position is reached, with at minimum a three-stent overlap (75 mm) with the proximal component. No part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall.
3. Check the graft position by angiography and adjust if necessary.
4. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned to the open position. (**Fig. 8**)
5. Stabilize the gray positioner (introduction system shaft) and begin withdrawing the sheath.

CAUTION: As the sheath is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check position as necessary.

NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.

6. Withdraw the sheath until the graft is fully expanded. Continue to withdraw the sheath until the valve assembly with the Captor Sleeve docks with the telescoping black gripper. (**Fig. 12**)
7. To release the distal attachment, hold the black gripper and turn the black safety-lock knob on the rotation handle in the direction of the arrow. Make sure the black safety-lock knob is in the unlocked position. (**Fig. 13**) Turn the blue rotation handle in the direction of the arrow next to label 1 until a stop is felt. (**Fig. 14**)

NOTE: If the blue rotation handle stops before completing the rotation, verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.

NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation handle will remain engaged. Continue with the procedure.

8. Turn the gray safety-lock knob, indicated by label 2, on the black sliding gripper in the direction of the arrow. (**Fig. 15**)

NOTE: Care should be taken to avoid landing the bare stent in regions of localized angulation > 45 degrees. If the bare stent is landed in localized angulations > 45 degrees, it may be difficult to release the bottom cap, as observed in the clinical study. Using a brachio-femoral wire guide technique can increase support of the system and ease the release of the bottom cap.

9. To release the distal bare stent, stabilize the introduction system and slide the black sliding gripper over the gray tube and outer sheath in a distal direction until it locks automatically into position next to the blue rotation handle. (**Fig. 16**) The release window on the handle next to label 3 will turn green. (**Fig. 17**) If the window has not turned green, slide the black sliding gripper until it locks with the blue rotation handle.
10. If the bare stent cannot be fully released from the cap, complete the deployment procedure and refer to **Section 13, RELEASE TROUBLESHOOTING**.
11. Turn the blue rotation handle in the direction of the arrow next to label 3 until a stop is felt and the proximal end of the graft opens.

If difficulty is encountered rotating the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

12. Remove the inner introduction system entirely, leaving the sheath and wire guide in place.
13. Close the Captor Hemostatic Valve on the Flexor Introducer Sheath by turning it to the closed position.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

11.1.4 Main Body Molding Balloon Insertion – Optional

1. Prepare the molding balloon as follows and/or per the manufacturer's instructions:
   - Flush the wire lumen with heparinized saline.
   - Remove all air from the balloon.
2. In preparation for insertion of the molding balloon, open the Captor Hemostatic Valve by turning it to the open position. (**Fig. 8**)
3. Advance the molding balloon over the wire guide and through the hemostatic valve of the main body introduction system to the level of the proximal fixation seal site. Maintain proper sheath positioning.
4. Tighten the Captor Hemostatic Valve around the molding balloon with gentle pressure by turning it to the closed position.

CAUTION: Do not inflate balloon in the aorta outside of the graft.

5. Expand the molding balloon with diluted contrast media (as directed by the manufacturer) in the area of the proximal covered stent, starting proximally and working in the distal direction.

CAUTION: Confirm complete deflation of balloon prior to repositioning.

6. If applicable, withdraw the molding balloon to the proximal component/ distal component overlap and expand.
7. Withdraw the molding balloon to the distal fixation site and expand.
8. Open the Captor Hemostatic Valve, remove the molding balloon and replace it with an angiographic catheter to perform completion angiograms.
9. Tighten the Captor Hemostatic Valve around the angiographic catheter with gentle pressure by turning it clockwise.
10. Remove or replace all stiff wire guides to allow the aorta to resume its natural position.

11.1.5 Final Angiogram

1. Position angiographic catheter just above the level of the endovascular graft. Perform angiography to verify correct positioning of the graft. Verify patency of arch vessels and celiac plexus.
2. In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers are positioned to provide adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.

NOTE: If endoleaks or other problems are observed (e.g., inadequate seal length or overlap length), refer to **Section 11.2, Ancillary Devices: Distal Extensions.**

3. Remove the sheaths, wires, and catheters.
4. Repair vessels and close in standard surgical fashion.

11.2 Ancillary Devices: Distal Extensions

General Use Information

Inaccuracies in device size selection or placement, changes or anomalies in patient anatomy, or procedural complications can require placement of additional endovascular grafts and extensions. Regardless of the device placed, the basic procedure(s) will be similar to the maneuvers required and described previously in this document. It is vital to maintain wire guide access.

Standard techniques for placement of arterial access sheaths, guiding catheters, angiographic catheters, and wire guides should be employed during use of the Zenith Alpha Thoracic Endovascular Graft ancillary devices.

The Zenith Alpha Thoracic Endovascular Graft ancillary devices are compatible with .035 inch diameter wire guides. Additional proximal main body components may be used to extend graft coverage proximally. Distal extensions are used to extend the distal body of an in situ endovascular graft or to increase the length of overlap between graft components.

11.2.1 Distal Extension Preparation/Flush

1. Remove the yellow-hubbed inner stylet from the dilator tip. Verify that the Captor Sleeve is within the Captor Hemostatic Valve; do not remove the Captor Sleeve. (**Fig. 5**)
2. Elevate distal tip of system and flush through the hemostatic valve until fluid exits the tip of the introducer sheath. (**Fig. 6**) Continue to inject a full 60 mL of flushing solution through the device. Discontinue injection and close the stopcock on the connecting tube.

NOTE: Graft flushing solution of heparinized saline is often used.

3. Attach a syringe with heparinized saline to the hub on the rotation handle. (**Fig. 7**) Flush until fluid exits the distal sideports and dilator tip.
4. Soak sterile gauze pads with saline and use to wipe the Flexor Introducer Sheath to activate the hydrophilic coating. Hydrate both sheath and dilator liberally.

11.2.2 Placement of the Distal Extension

1. Puncture the selected artery using standard technique with an 18 gage access needle. Alternatively, use the in situ wire guide that was used previously for introduction system/graft insertions. Upon vessel entry, insert:
   - Wire guide – standard .035 inch, 260/300 cm, 15 mm J tip or Bentson wire guide
   - Appropriate size sheath (e.g., 5 French)
   - Pigtail flush catheter (often radiopaque-banded sizing catheters; e.g., Cook Centimeter Sizing CSC-20 catheter
2. Perform angiography at the appropriate level. If using radiopaque markers, adjust position as necessary and repeat angiography.
3. Ensure the graft system has been primed with heparinized saline, and all air has been removed.
4. Give systemic heparin. Flush all catheters and wire guides with heparinized saline. Reflush catheters and rewet wire guides after each exchange.
5. Replace the standard wire guide with a stiff .035 inch, 260/300 cm, LESDC wire guide and advance it through the catheter and up to the aortic arch.
6. Remove the pigtail flush catheter and sheath.

NOTE: At this stage, the second femoral artery can be accessed for flush catheter placement. Alternatively, consider using a brachial approach.

7. Introduce the freshly hydrated introduction system over the wire guide and advance until the desired graft position is reached. Ensure that the distal extension overlaps the distal component by a minimum of three stents (plus the distal uncovered stent).

CAUTION: To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.

NOTE: The dilator tip softens at body temperature.

NOTE: To facilitate introduction of the wire guide into the introduction system, it may be necessary to slightly straighten the introduction system dilator tip.

8. Verify wire guide position in the aortic arch. Ensure correct graft position.
9. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned counterclockwise to the open position. (**Fig. 8**)
10. Stabilize the gray positioner (introduction system shaft) and withdraw the sheath until the graft is fully expanded and the valve assembly with the Captor Sleeve docks with the black gripper. (**Fig. 9**)

CAUTION: As the sheath or wire guide is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check position as necessary.

NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.

11. Verify graft position and, if necessary, adjust it forward. Recheck graft position with angiography.
12. While holding the black gripper, turn the black safety-lock knob in the direction of the arrow to engage the blue rotation handle. (**Fig. 10**) Make sure the black safety-lock knob is in the unlocked position.
13. Under fluoroscopy, turn the blue rotation handle in the direction of the arrow until a stop is felt. (**Fig. 11**) This indicates that the proximal end of the graft has opened, and that the distal attachment to the introducer has been released.

NOTE: If the blue rotation handle stops before completing the rotation, verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.

NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation handle will remain engaged. Continue with the procedure.

NOTE: If difficulty is still encountered during rotating the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

14. Remove the inner introduction system entirely, leaving the sheath and wire guide in place.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

15. Close the Captor Hemostatic Valve on the Flexor Introducer Sheath by turning it in a clockwise direction until it stops.

11.2.3 Distal Extension Molding Balloon Insertion – Optional

1. Prepare the molding balloon as follows and/or per the manufacturer's instructions:
   - Flush the wire lumen with heparinized saline.
   - Remove all air from the balloon.
2. In preparation for insertion of the molding balloon, open the Captor Hemostatic Valve by turning it counterclockwise. (**Fig. 8**)
3. Advance the molding balloon over the wire guide and through the Captor

Hemostatic Valve of the introduction system to the level of the distal component/distal extension overlap. Maintain proper sheath positioning.

4. Tighten the Captor Hemostatic Valve around the molding balloon with gentle pressure by turning it clockwise.
   CAUTION: Do not inflate balloon in the aorta outside of the graft.
5. Expand the molding balloon with diluted contrast media (as directed by the manufacturer) in the area of the overlap, starting proximally and working in the distal direction.
   CAUTION: Confirm complete deflation of balloon prior to repositioning.
6. Withdraw the molding balloon to the distal fixation site and expand.
7. Loosen the Captor Hemostatic Valve, remove the molding balloon and replace it with an angiographic catheter to perform completion angiograms.
8. Tighten the Captor Hemostatic Valve around the angiographic catheter with gentle pressure by turning it clockwise.
9. Remove or replace all stiff wire guides to allow aorta to resume its natural position.

11.2.4 Final Angiogram

1. Position angiographic catheter just above the level of the endovascular graft. Perform angiography to verify correct positioning. Verify patency of arch vessels and celiac plexus.
2. In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers are positioned to provide adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.
   NOTE: If endoleaks or other problems are observed (e.g., inadequate seal length or overlap length), refer to **Section 11.2, Ancillary Devices: Distal Extensions.**
3. Remove the sheaths, wires, and catheters.
4. Repair vessels and close in standard surgical fashion.

12 IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP

12.1 General

- **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the endovascular graft) should receive additional follow-up. Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be told that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of thoracic lesions.
- Physicians should evaluate patients on an individual basis and prescribe their follow-up relative to the needs and circumstances of each individual patient. The recommended imaging schedule is presented in **Table 3**. This schedule continues to be the minimum requirement for patient follow-up and should be maintained even in the absence of clinical symptoms (e.g., pain, numbness, weakness). Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the stent graft) should receive follow-up at more frequent intervals.
- Annual imaging follow-up should include thoracic device radiographs and both contrast and non-contrast CT examinations. If renal complications or other factors preclude the use of image contrast media, thoracic device radiographs and non-contrast CT may be used in combination with transesophageal echocardiography for assessment of endoleak.
- The combination of contrast and non-contrast CT imaging provides information on device migration, aneurysm diameter or ulcer depth change, endoleak, patency, tortuosity, progressive disease, fixation length, and other morphological changes.
- The thoracic device radiographs provide information on device migration and device integrity (separation between components, stent fracture, and barb separation) that may or may not be visible on CT depending on the quality of the scan.

Table 3 lists the minimum requirements for imaging follow-up for patients with the Zenith Alpha Thoracic Endovascular Graft. Patients requiring enhanced follow-up should have interim evaluations.

Table 3 – Recommended Imaging Schedule for Endograft Patients

	Angiogram	CT (contrast and non-contrast)	Thoracic Device Radiographs
Pre-procedure		X[1]	
Procedural	X		
1 month		X[2]	X
6 month		X[2]	X
12 month (annually thereafter)		X[2]	X

[1] Imaging should be performed within 6 months before the procedure.

[2] MR imaging may be used for those patients experiencing renal failure of who are otherwise unable to undergo contrast-enhanced CT, with transesophageal echocardiography being an additional option in the event of suboptimal MR imaging. For Type I or III endoleak, prompt intervention and additional follow-up post-intervention is recommended. See **Section 12.5, Additional Surveillance and Treatment**.

12.2 Contrast and Non-Contrast CT Recommendations

- Image sets should include all sequential images at lowest possible slice thickness (≤ 3 mm). Do NOT perform large slice thickness (> 3 mm) and/or omit consecutive CT image sets, as it prevents precise anatomical and device comparisons over time
- The same scan parameters (i.e., spacing, thickness, and FOV) should be used at each follow-up. Do not change the scan table x- or y- coordinates while scanning.
- Sequences must have matching or corresponding table positions. It is important to follow acceptable imaging protocols during the CT exam. **Table 4** lists examples of acceptable imaging protocols.

Table 4 – Acceptable Imaging Protocols

	Non-contrast	Contrast
IV contrast	No	Yes
Acceptable machines	Spiral CT or high performance MDCT capable of > 40 seconds	Spiral CT or high performance MDCT capable of > 40 seconds
Injection volume	n/a	Per institutional protocol
Injection rate	n/a	> 2.5 mL/sec
Injection mode	n/a	Power
Bolus timing	n/a	Test bolus: Smart Prep, C.A.R.E. or equivalent
Coverage - start	Neck	Subclavian aorta Coverage
- finish	Diaphragm	Profunda femoris origin
Collimation	< 3 mm	< 3 mm
Reconstruction	2.5 mm throughout - soft algorithm	2.5 mm throughout - soft algorithm
Axial DFOV	32 cm	32 cm
Post-injection runs	None	None

12.3 Thoracic Device Radiographs

The following films are required: supine-frontal (AP), cross-table lateral, 30 degree RPO, and 30 degree LPO.

Follow the following protocols during each examination:

- Record the table-to-film distance and use the same distance at each subsequent examination.
- Ensure entire device is captured on each single image format lengthwise.
- The middle photocell, thoracic spine technique, or manual technique should be used for all views to ensure adequate penetration of the mediastinum.

If there is any concern about the device integrity (e.g., kinking, stent breaks, barb separation, relative component migration), it is recommended to use magnified views. The attending physician should evaluate films for device integrity (entire device length, including components) using 2-4x magnification visual aid.

Mail:	MedicAlert Foundation International 2323 Colorado Avenue Turlock, CA 95382
Phone:	888-633-4298 (toll free) 209-668-3333 from outside the US
Fax:	209-669-2450
Web:	www.medicalert.org

12.4 MRI Safety Information

Nonclinical testing has demonstrated that the Zenith Alpha Thoracic Endovascular Graft is MR Conditional according to ASTM F2503. A patient with this endovascular graft can be scanned safely after placement under the following conditions.

- Static magnetic field of 1.5 or 3.0 tesla.
- Maximum spatial magnetic field of 1600 gauss/cm (16.0 T/m)or less
- Maximum MR system reported, whole-body-averaged specific absorption rate (SAR) of ≤ 2 W/kg (normal operating mode) for 15 minutes of continuous scanning

Under the scan conditions defined above, the Zenith Alpha Thoracic Endovascular Graft is expected to produce a maximum temperature rise of less than 2.1°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 5 mm from the Zenith Alpha Thoracic Endovascular Graft when imaged with a gradient echo pulse sequence and a 3.0 T MR system. The image artifact obscures a portion of the device lumen.

For U.S. Patients Only

Cook recommends that the patient register the MR conditions disclosed in this IFU with the MedicAlert Foundation. The MedicAlert Foundation can be contacted in the following manners:

12.5 Additional Surveillance and Treatment

(Refer to **Section 4, WARNINGS AND PRECAUTIONS**)

Additional surveillance and possible treatment is recommended for:

- Type I endoleak
- Type III endoleak
- Aneurysm or ulcer enlargement, ≥ 5 mm of maximum aneurysm diameter or ulcer depth (regardless of endoleak status)
- Migration
- Inadequate seal length
- Graft thrombosis or occlusion
- Loss of device integrity
  - Barb separation
  - Stent fracture
  - Relative component migration

Consideration for reintervention or conversion to open repair should include the attending physician's assessment of an individual patient's comorbidities, life expectancy, and the patient's personal choices. Patients should be counseled that subsequent reinterventions, including catheter-based and open surgical conversion, are possible following endograft placement.

13 RELEASE TROUBLESHOOTING

NOTE: Technical assistance from a Cook product specialist may be obtained by contacting your local Cook representative.

13.1 Difficulty Removing Release Wires

Turning the rotation handle pulls the release wire back, releasing the stent graft attachment to the introducer. If the stent graft is not completely released, it is possible to disassemble the rotation handle by following the steps below.

1. Use surgical forceps to pull the back-end clips out (**Fig. 18** and **19**) and remove the back-end cap. (**Fig. 20**)
2. Stabilize the gray positioner and slide the blue rotation handle backward to pull the release wires until the graft is released. Do not pull the release wires completely out of the rotation handle. (**Fig. 21** and **22**)
3. If leakage thought the valve occurs, remove the inner introduction system entirely, leaving the sheath and wire guide in place.
4. Close the Captor Hemostatic Valve on the Flexor introducer sheath by turning it to the closed position.

   NOTE: If extreme force is needed, wind the release wires around the surgical forceps. (**Fig. 23**)

13.2 Distal Component - Bare Stent Deployment

If the bare stent cannot be fully deployed from the cap: (**Fig. 24**)

1. Advance the Flexor sheath to the distal edge of the stent graft. (**Fig. 25** and **26**)
2. Stabilize the Flexor sheath and pull back the blue rotation handle. (**Fig. 27**)

The bare stent will now be released from the cap but still be inside the sheath. Withdraw the sheath **SLOWLY** with a rotating movement (**Fig. 28**) until the bare stent is outside the sheath.

Manufacturer
WILLIAM COOK EUROPE ApS
Sandet 6, DK-4632
Bjaeverskov, DENMARK

www.cookmedical.com

2015-02
I-ALPHA-THORACIC-438-0

6. Summary of Clinical Data

The Zenith Alpha™ Thoracic Endovascular Graft is indicated for the endovascular treatment of patients with isolated lesions of the descending thoracic aorta (not including dissections) having vascular anatomy suitable for endovascular repair.

The Zenith Alpha™ Thoracic Endovascular Graft has been the subject of several documented clinical evaluations, including two pivotal studies (one international) that evaluated the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft in patients with thoracic aneurysm/ulcer and blunt thoracic aortic injury, as summarized in Table 6-1. Additional clinical evaluations include a continued access study for the aneurysm/ulcer indication (see Section 6.3.2) and a European post-market survey (see Section 6.3.3) to further confirm performance of a user interface modification to the introduction system (rotation handle).

Table 6-1. Summary of primary pivotal studies

Pivotal Study	Study Design	Objective	Number of Sites with Enrollment	Number of Patients
Aneurysm/ Ulcer	Prospective, nonrandomized, single-arm, multinational (US, Japan, Germany, England, Sweden) study	To evaluate safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with aneurysms/ulcers of the descending thoracic aorta.	23	110
BTAI	Prospective, nonrandomized, noncomparative, single-arm, US multicenter study	To evaluate safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of BTAI	17	50

6.1. Clinical Study for the Aneurysm/Ulcer Indication

The Zenith Alpha™ Thoracic Endovascular Graft clinical study was a prospective, nonrandomized, single-arm, multinational study that was conducted to evaluate the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with aneurysms/ulcers of the descending thoracic aorta. Patients were treated between March 17, 2010 (first US enrollment on October 1, 2010) and January 16, 2013. The data presented herein was collected on 110 patients through April 7, 2015. There were 23 investigational sites, including centers in the US (51 patients at 14 sites), Japan (43 patients at 3 sites), Germany (13 patients at 4 sites), Sweden (3 patients at 1 site), and England (1 patient at 1 site). The presenting anatomy, based on core laboratory analysis

of pre-procedure imaging, was a thoracic aneurysm in 81.8% (90/110) of patients and a thoracic ulcer in 18.2% (20/110) of patients.

The pivotal study endpoints were established based on performance goals derived from the pivotal study of the previous device, the Zenith® TX2® TAA Endovascular Graft. Similar inclusion/exclusion criteria were used between the two studies. A post hoc analysis was performed comparing demographic, comorbid, and baseline anatomical characteristics between the present study and the previous Zenith® TX2® TAA Endovascular Graft study used to derive the performance goals for hypothesis testing. Of the few variables that were found to be different between studies, none appeared to be relevant with respect to assessing the safety and effectiveness endpoints, thus confirming that comparing to performance goals derived from the previous study remained appropriate.

The primary safety endpoint was 30-day freedom from major adverse events (MAEs), and the performance goal was 80.6%. MAEs were defined as the following: all-cause death; Q-wave MI; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

The primary effectiveness endpoint was device success at 12-month. Device success at 12 months was defined as: Technical Success, with none of the following at 12 months:

- Type I or type III endoleaks requiring re-intervention
- Aneurysm rupture or conversion to open surgical repair
- Aneurysm enlargement greater than 0.5 cm

Technical success was defined as successful access of the aneurysm site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location. The endovascular graft must be patent at the time of deployment completion as evidenced by intraoperative angiography.

The effectiveness hypothesis of the study was that device success at 12 months met the performance goal of 80.7%.

An independent core laboratory analyzed all patient imaging. An independent clinical events committee (CEC) adjudicated all major adverse events (MAEs), including all patient deaths; additionally the CEC also adjudicated core laboratory reports of migration and device integrity loss. An independent data safety monitoring board (DSMB) monitored the clinical trial according to an established safety monitoring plan.

The study follow-up schedule (Table 6.1-1) consisted of both clinical and imaging (CT and X-ray) assessments at post-procedure (pre-discharge), 30 days, 6 months, 12 months, and yearly thereafter through 5 years.

Table 6.1-1. Study follow-up schedule

Study Schedule							
	Pre-op	Intra-op	Post-procedure	30-Day	6-Month	12-Month	24-Month[d]
Clinical exam	X		X	X	X	X	X
Blood tests	X		X	X	X	X	X
CT scan	X[a]			X[c]	X[c]	X[c]	X[c]
Thoracic x-ray				X	X	X	X
Angiography	X[b]	X					

[a]It is recommended that imaging be performed within 6 months before the procedure.
[b]Required only to resolve any uncertainties in anatomical measurements necessary for graft sizing.
[c]MR imaging may be used for those patients experiencing renal failure or who are otherwise unable to undergo contrast-enhanced CT scan, with TEE being an additional option in the event of suboptimal MR imaging.
[d]Yearly thereafter through 5 years.

At the time of the database lock, of 110 patients enrolled in the study, 90% (99/110) were eligible for follow-up at 12 months (Table 6.1-2). All patients were evaluable for the primary safety endpoint (freedom from MAE at 30 days). All patients were also evaluable for the primary effectiveness endpoint (12-month device success) based on a component of the composite measure having been assessed at the time of the procedure, consistent with the performance goal development. Two patients, although enrolled in the study, did not receive the device due to an inability to advance/gain access to the target treatment site. Although the primary safety and effectiveness endpoints were evaluated at 30 days and 12 months, respectively, patient data presented herein include longer-term follow-up that was available at the time of the data lock (April 7, 2015). Table 6.1-2 reports the percent of follow-up data available through 4 years.

Table 6.1-2. Follow-up availability

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]				Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Patients with Data for that Visit	CT[c]	X-ray	Patients with Follow-up Pending[d]	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
Operative	110	110/110 (100%)	NA	NA	0	NA	NA	NA	NA	0	0	0	0
30-day	110[e]	106/110 (96.4%)	105/108 (97.2%)	98/108 (90.7%)	0	105/108 (97.2%)	102/108 (94.4%)	NA	105/108 (97.2%)	3	0	0	2[e]
6-month	105	99/105 (94.3%)	97/105 (92.4%)	92/105 (87.6%)	0	96/105 (91.4%)	91/105 (86.7%)	94/105 (89.5%)	98/105 (93.3%)	2	0	4	0
12-month	99	91/99 (91.9%)	92/99 (92.9%)	84/99 (84.8%)	0	92/99 (92.9%)	83/99 (83.8%)	92/99 (92.9%)	92/99 (92.9%)	7	1	2	0
2-year	89	78/89 (87.6%)	79/89 (88.8%)	75/89 (84.3%)	8	77/89 (86.5%)	73/89 (82.0%)	77/89 (86.5%)	77/89 (86.5%)	3	0	7	45
3-year	34	23/34 (67.6%)	20/34 (58.8%)	18/34 (52.9%)	11	17/34 (50.0%)	15/34 (44.1%)	17/34 (50.0%)	17/34 (50.0%)	0	0	0	26
4-year	8	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	2	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	0	0	0	8

NA – Not assessed.
LTF/WTHD – Lost-to-follow-up and withdrawn.
[a]Site-submitted data.
[b]Based on core laboratory analysis.
[c]Includes MRI or TEE imaging (which is allowed per protocol) when the patient is unable to receive contrast medium due to renal failure.
[d]Patients still within follow-up window, but data not yet available.
[e]Two patients did not receive the device at the time of the implant procedure and therefore only 30-day clinical follow-up was applicable before the patients exited the study, with no further follow-up due thereafter.

Demographics and Patient Characteristics

The demographics and patient characteristics are presented in Table 6.1-3.

Table 6.1-3. Demographics and patient characteristics

Demographic	Mean ± SD (n, range) or Percent Patients (number/total number)
Age (years)	
All patients	72.2 ± 9.8 (n=110, 42 – 92)
Male	70.7 ± 9.9 (n=64, 42 – 85)
Female	74.3 ± 9.4 (n=46, 44 – 92)
Gender	
Male	58.2% (64/110)
Female	41.8% (46/110)
Ethnicity	
White	53.6% (59/110)
Hispanic or Latino	0
Black or African American	8.2% (9/110)
American Indian or Alaska Native	0
Asian	38.2% (42/110)
Native Hawaiian or other Pacific Islander	0
Other	0
Height (in)	65.3 ± 4.5 (n=110, 55.1 – 75.2)
Weight (lbs)	161.7 ± 44.3 (n=110, 79.2 – 330.0)
Body mass index	26.5 ± 6.0 (n=110, 16.4 – 50.0)

The medical history and comorbid medical conditions for the patient cohort are presented in Table 6.1-4.

Table 6.1-4. Pre-existing comorbid medical conditions

Medical History	Percent Patients (number/total number)
Cardiovascular	
Myocardial infarction (MI)	12.7% (14/110)
Angioplasty/stent	10.0% (11/110)
Cardiac or thoracic surgery	16.4% (18/110)
Prior diagnosis of symptomatic congestive heart failure (CHF)	10.0% (11/110)
Angina	16.4% (18/110)
Prior diagnosis of arrhythmia	23.6% (26/110)
Hypertension	88.2% (97/110)
Coronary artery bypass graft	11.8% (13/110)

Medical History	Percent Patients (number/total number)
Vascular	
Thromboembolic event	0.9% (1/110)
Peripheral vascular disease	21.8% (24/110)
Symptomatic carotid disease warranting intervention	1.8% (2/110)
Any aneurysm (other than the study lesion)	45.5% (50/110)
Thoracic aortic aneurysm	2.7% (3/110)
Abdominal aortic aneurysm	26.4% (29/110)
Other aneurysm[a]	16.4% (18/110)
Degenerative or atherosclerotic ulcer (other than the study lesion)	0.9% (1/110)
Any dissection	9.1% (10/110)[b]
Thoracic aortic dissection	6.4% (7/110)[c]
Abdominal aortic dissection	0
Other dissection[d]	2.7% (3/110)
Thoracic trauma	3.6% (4/110)[e]
Aortobronchial fistula	0.9% (1/110)
Aortoesophageal fistula	0
Bleeding diathesis or uncorrectable coagulopathy	0
Endarterectomy	1.8% (2/110)
Diagnosed or suspected congenital degenerative collagen disease	0
Pulmonary	
Chronic obstructive pulmonary disease (COPD)	25.5% (28/110)
Home oxygen	1.8% (2/110)
Renal	
Chronic renal failure	10.0% (11/110)
Hemodialysis	1.8% (2/110)
Chronic peritoneal dialysis	0
Endocrine	
Diabetes	19.1% (21/110)
Hypercholesterolemia	73.6% (81/110)
Infectious disease	
Systemic infection	0
Gastrointestinal	
Gastrointestinal disease	34.5% (38/110)
Hepatobiliary	
Liver disease	12.7% (14/110)
Neoplasms	
Cancer	24.5% (27/110)
Neurologic	
Stroke	10.9% (12/110)
Substance use	
Past or current smoker	71.8% (79/110)
Allergies	
Allergies	41.8% (46/110)

[a]The "other" aneurysm category includes patients with aneurysms in different locations (i.e., not descending thoracic or abdominal aorta) and patients with aneurysms in multiple locations.
[b]All patients had a history of aortic dissection but at the time of enrollment had no radiographic evidence of aortic dissection.
[c]The treated aneurysm/ulcer was located in the same aortic segment as the previously diagnosed dissection in four patients.
[d]The "other" dissection category includes patients with dissection in different locations (i.e., not descending thoracic or abdominal aorta) and patients with dissections in multiple locations.
[e]All patients had a history (> 1 year) of traumatic thoracic injury.

Table 6.1-5 reports the ASA classification.

Table 6.1-5. ASA physical status classification

ASA Classification	Percent Patients (number/total number)
Healthy patient (1)	8.2% (9/110)
Mild systemic disease (2)	55.5% (61/110)
Severe systemic disease (3)	26.4% (29/110)
Incapacitating systemic disease (4)	10.0% (11/110)
Moribund patient (5)	0

Table 6.1-6 reports the SVS-ISCVS risk score.

Table 6.1-6. SVS-ISCVS risk score classification

SVS-ISCVS Category	Percent Patients (number/total number)
Diabetes risk score	
0	83.6% (92/110)
1	5.5% (6/110)
2	9.1% (10/110)
3	1.8% (2/110)
4	0
Smoking risk score	
0	47.3% (52/110)
1	30.0% (33/110)
2	13.6% (15/110)
3	9.1% (10/110)
Hypertension risk score	
0	11.8% (13/110)
1	29.1% (32/110)
2	31.8% (35/110)
3	27.3% (30/110)
Hyperlipidemia risk score	
0	26.4% (29/110)
1	17.3% (19/110)
2	1.8% (2/110)
3	54.5% (60/110)
Cardiac status risk score	
0	70.0% (77/110)
1	18.2% (20/110)
2	11.8% (13/110)
3	0
Carotid disease risk score	
0	84.5% (93/110)
1	13.6% (15/110)
2	0.9% (1/110)
3	0.9% (1/110)

SVS-ISCVS Category	Percent Patients (number/total number)
Renal status risk score	
0	87.3% (96/110)
1	10.9% (12/110)
2	0
3	1.8% (2/110)
Pulmonary status risk score	
0	66.4% (73/110)
1	26.4% (29/110)
2	6.4% (7/110)
3	0.9% (1/110)
Total SVS/ISCVS risk score	5.9 ± 2.6 (n=110, 1 – 14)

The majority of patients (81.8%) had fusiform aneurysms and the remaining 18.2% had penetrating atherosclerotic ulcers. Table 6.1-7 reports the presenting morphology.

Table 6.1-7. Presenting morphology type per the core laboratory

Morphology	Percent Patients (number/total number)
Aneurysm	81.8% (90/110)
Ulcer	18.2% (20/110)

Table 6.1-8 reports presenting anatomical dimensions of the aneurysm/ulcer, the proximal and distal aortic necks, and the right and left iliac arteries.

Table 6.1-8. Presenting anatomical dimensions reported per the core laboratory

Measure	Mean ± SD (n, range)
Aneurysm dimensions	
Major diameter (mm)	60.9 ± 11.4 (n=90, 41 – 99)
Minor diameter (mm)	51.7 ± 11.1 (n=90, 30 – 92)
Length (mm)	113.5 ± 63.0 (n=90, 25.4 – 324.0)
Ulcer dimensions	
Ulcer depth (mm)	14.1 ± 3.7 (n=20, 8 – 25)
Length (mm)	34.8 ± 20.3 (n=20, 11.0 – 85.7)
Proximal neck diameter	
Left common carotid artery	
Major (mm)	34.0 ± 3.0 (n=110, 24 – 42)
Minor (mm)	31.1 ± 3.5 (n=110, 18 – 39)
20 mm distal to left common carotid artery	
Major (mm)	33.3 ± 4.3 (n=110, 22 – 54)
Minor (mm)	30.6 ± 4.3 (n=110, 20 – 49)
Distal neck diameter	
20 mm proximal to celiac artery	
Major (mm)	31.0 ± 5.1 (n=110, 20 – 48)
Minor (mm)	28.9 ± 4.7 (n=110, 19 – 42)
Celiac artery	
Major (mm)	29.5 ± 4.4 (n=110, 20 – 44)

Measure	Mean ± SD (n, range)
Minor (mm)	27.3 ± 3.8 (n=110, 19 – 38)
Proximal neck length Left common carotid artery to distal part of neck (mm)	94.7 ± 57.8 (n=110, 14.4 – 276.7)
Distal neck length Celiac artery to proximal part of neck (mm)	105.2 ± 63.2 (n=110, 5.6 – 268.5)
Right iliac artery diameter Narrowest segment (mm)	6.7 ± 1.6 (n=105, 3 – 10)[a]
Left iliac artery diameter Narrowest segment (mm)	6.9 ± 1.8 (n=104, 0 – 11)[a]

[a]CT imaging was not always adequate for measurement of the iliac arteries.

Table 6.1-9 reports the distribution in aneurysm diameter/ulcer depth.

Table 6.1-9. Distribution in range of maximum aneurysm diameter or ulcer depth per the core laboratory

Type	Size Range[a]	Percent Patients (number/total number)
Aneurysm	40 mm – < 50 mm	8.9% (8/90)
	50 mm – < 60 mm	40.0% (36/90)
	60 mm – < 70 mm	36.7% (33/90)
	70 mm – < 80 mm	6.7% (6/90)
	80 mm – < 90 mm	4.4% (4/90)
	90 mm – < 100 mm	3.3% (3/90)
Ulcer	< 20 mm	95.0% (19/20)
	20 mm – < 30 mm	5.0% (1/20)
	30 mm – < 40 mm	0
	40 mm – < 50 mm	0
	50 mm – < 60 mm	0
	60 mm – < 70 mm	0
	70 mm – < 80 mm	0

[a]Diameter for aneurysms and depth for ulcers.

Table 6.1-10 provides the distribution in location of the aneurysm/ulcer.

Table 6.1-10. Location of the primary aneurysm/ulcer as determined by the core laboratory

Location	Percent Patients (number/total number)		
	Aneurysm Patients	Ulcer Patients	All Patients
Location in the thoracic aorta			
Proximal	26.7% (24/90)	50.0% (10/20)	30.9% (34/110)
Middle	53.3% (48/90)	30.0% (6/20)	49.1% (54/110)
Distal	20.0% (18/90)	20.0% (4/20)	20.0% (22/110)

Procedural Information

The majority (71.8%) of procedures were performed under general anesthesia, followed by local anesthesia in 21.8% of procedures. Vascular access was gained via femoral artery cutdown in 62.7% of patients, percutaneously in 36.4% of patients and by using a conduit 0.9% of patients. The mean procedure time was 99.4 ± 53.6 minutes (range 31-362) and the mean procedural blood loss was 121.8 ± 137.7 ml. The mean anesthesia time was 162.7 ± 61.4 minutes and the mean fluoroscopy time was 20.0 ± 20.1 minutes.

Adjunctive procedures for spinal cord protection to prevent paraplegia were performed in 40.0% of patients (72.7% of the adjunctive procedures were cerebral spinal fluid (CSF) drainage), and induced hypotension to ease deployment was performed in 7.3% of patients. The left subclavian artery (LSA) was covered completely in 13% of patients. No LCCA to LSA bypass or LSA transposition were performed.

The access method used to insert the Zenith Alpha™ Thoracic Endovascular Graft is presented in Table 6.1-11. Three types of methods were used: percutaneous (direct needle puncture of the access vessel), cutdown (surgical exposure of the access vessel), and conduit (surgical technique used to bypass prohibitive access vessels). For the percutaneous access method, the procedure time was 88.8 ± 44.7 minutes, blood loss was 128.5 ± 136.4 cc, and incidence of access site complications was 7.3%. For the cutdown/conduit access method, the procedure time was 105.4 ± 57.6 minutes, blood loss was 118.0 ± 139.3 cc, and incidence of access site complications was 5.7%. These data support the use of either method of access for the device.

Table 6.1-11. Access method used to insert the endovascular graft

Type	Percent Patients (number/total number)		
	Aneurysm Patients	**Ulcer Patients**	**All Patients**
Percutaneous	31.1% (28/90)	60.0% (12/20)	36.4% (40/110)
Cutdown	67.8% (61/90)	40.0% (8/20)	62.7% (69/110)
Conduit	1.1% (1/90)	0	0.9% (1/110)

The location of the graft components relative to an identified site is provided as percent of patients in Table 6.1-12.

Table 6.1-12. Graft location per core laboratory

Location	Percent Patients (number/total number)		
	Aneurysm Patients	Ulcer Patients	All Patients
Proximal aspect of graft			
Above LCCA	0	0	0
Below LCCA, above LSA	9.1% (8/88)	30.0% (6/20)	13.0% (14/108)
Below LSA	83.0% (73/88)	60.0% (12/20)	78.7% (85/108)
Unable to assess[a]	8.0% (7/88)	10.0% (2/20)	8.3% (9/108)
Distal aspect of graft			
Above celiac artery	95.5% (84/88)	90.0% (18/20)	94.4% (102/108)
Below celiac artery	0	0	0
Unable to assess[a]	4.5% (4/88)	10.0% (2/20)	5.6% (6/108)

LCCA = left common carotid artery; LSA = left subclavian artery.
[a]All patients had post-procedure angiography but not all imaging was adequate for core laboratory review.

Two patients required axillary-axillary bypasses prior to the index procedure (both from a Japanese site). Additional procedures performed after graft deployment included use of a vessel closure device in 26 patients, LCCA stent placement in 1 patient, LSA stent in 1 patient, LSA coil embolization in 5 patients, femoral endarterectomy in 2 patients, thrombo-endarterectomy and patch right femoral in1 patient, iliac artery stents in 3 patients, and chimney stent to maintain blood flow to the LCCA and LSA coil embolization in one patient. Table 6.1-13 reports additional procedures performed either before or after graft implantation.

Table 6.1-13. Additional procedures

Procedure	Percent Patients (number/total number)	
	Before Graft Deployment	After Graft Deployment
Left carotid artery stent	0	0.9% (1/110)
Left subclavian artery stent	0	0.9% (1/110)
Iliac artery angioplasty	0.9% (1/110)	0
Iliac artery stent	0	2.7% (3/110)
Vessel closure device	0	23.6% (26/110)
Other	1.8% (2/110)[a]	8.2% (9/110)[b]

[a]Two patients from Japan (1040051 and 1040069) underwent axillary-axillary bypass prior to the index procedure.
[b]Two patients (1030005 and 1030044) underwent right femoral endarterectomy after the index procedure. One patient (0465997) underwent thromboendarterectomy and patch right femoral after the index procedure. Five patients (1040023, 1040033, 1040039, 1040051, and 1040069) underwent coil embolization of the left subclavian artery after the index procedure. One patient (1040080) had a chimney stent placed to maintain blood flow to the left common carotid artery and coil embolization of the left subclavian artery after the index procedure.

The device was successfully implanted in 98.2% of patients (2 patients did not receive the device due to the inability to insert/advance the introduction system) and all patients

(100%) survived the endovascular procedure. Overall, the procedural results were as expected for the treatment of patients with aneurysms or ulcers of the descending thoracic aorta.

Clinical Utility Measures

The clinical utility results are presented in Table 6.1-14.

Table 6.1-14. Clinical utility measures

Clinical Utility Measure	Mean ± SD (n, range)[a]		
	Aneurysm	Ulcer	All patients
Duration of ICU stay (days)	2.6 ± 9.9 (n=88, 0 – 91)	0.8 ± 0.6 (n=20, 0 – 2)	2.3 ± 8.9 (n=108, 0 – 91)
Days to resumption of oral fluid intake	0.4 ± 0.6 (n=89, 0 – 3)	0.5 ± 0.8 (n=20, 0 – 3)	0.4 ± 0.6 (n=109, 0 – 3)
Days to resumption of regular diet	1.3 ± 1.1 (n=89, 0 – 6)	1.5 ± 3.1 (n=19, 0 – 14)	1.3 ± 1.6 (n=108, 0 – 14)
Days to resumption of bowel function	2.3 ± 1.5 (n=70, 0 – 8)	2.0 ± 2.1 (n=15, 0 – 8)	2.3 ± 1.6 (n=85, 0 – 8)
Days to ambulation	1.6 ± 1.3 (n=88, 0 – 9)	1.8 ± 2.2 (n=20, 0 – 10)	1.6 ± 1.5 (n=108, 0 – 10)
Days to hospital discharge	7.4 ± 19.6 (n=90, 1 – 185)	5.0 ± 5.3 (n=20, 1 – 19)	7.0 ± 17.8 (n=110, 1 – 185)

[a]Not all clinical utility measures were assessed for all 110 patients.

Devices Implanted

Table 6.1-15 shows the percent of patients who received each type of Zenith Alpha™ Thoracic Endovascular Graft component (proximal, distal, or distal extension) during the initial implant procedure. Also included is the graft diameter range implanted for each component type.

Table 6.1-15. Stent-graft component type deployed

Type	Percent Patients (number/total number)[a]			Graft Diameter Range (All Patients)
	Aneurysm Patients	Ulcer Patients	All patients	
Proximal component (nontapered or tapered)	100% (88/88)	100% (20/20)	100% (108/108)	28 to 46 mm
Distal component	37.5% (33/88)	0	30.6% (33/108)	32 to 46 mm

Ancillary component	27.3% (24/88)[b]	5.0% (1/20)	23.1% (25/108)	28 to 46 mm
Additional proximal component	13.6% (12/88)	5.0% (1/20)	12.0% (13/108)	
Distal extension	14.8% (13/88)[c]	0	12.0% (13/108)	

[a]Two aneurysm patients did not receive a device as the introduction system could not be successfully advanced; therefore, the denominator is 108, not 110.
[b]One patient received both an additional proximal component and a distal extension.
[c]Includes 12 patients who received 1 distal extension, and 1 patient who received 2 distal extensions.

Table 6.1-16 further summarizes the total number of components placed during the initial implant procedure.

Table 6.1-16. Total number of components placed during the initial implant procedure

Main Body Design	Percent Patients (number/total number)[a]		Percent Patients (number/total number)		
			1	2	3
One-piece (proximal only)	Aneurysm Patients	62.5% (55/88)	69.1% (38/55)	29.1% (16/55)	1.8% (1/55)
	Ulcer Patients	100% (20/20)	95.0% (19/20)	5.0% (1/20)	0
	All Patients	69.4% (75/108)	76.0% (57/75)	22.7% (17/75)	1.3% (1/75)
Two-piece (proximal and distal)	Aneurysm Patients	37.5% (33/88)	N/A	78.8% (26/33)	21.2% (7/33)
	Ulcer Patients	N/A	N/A	N/A	N/A
	All Patients	30.6% (33/108)	N/A	78.8% (26/33)	21.2% (7/33)

[a]Two aneurysm patients did not receive a device as the introduction system could not be successfully advanced; therefore, the denominator is 108, not 110.

Table 6.1-17 reports the sizes (diameters and lengths) of the nontapered proximal components used during the initial implant procedure.

Table 6.1-17. Diameters and lengths of nontapered proximal component (ZTLP-P) sizes used

Diameter (mm)	Length (mm)	n
28	132	2
	155	2
30	132	8
	155	2
32	132	7
	155	4
	201	5
34	137	3
	161	6
	209	2
36	137	10
	161	6
	209	1

Diameter (mm)	Length (mm)	n
38	142	7
	167	3
	217	6
40	142	2
	167	3
	217	1
42	121	3
	173	4
44	125	2
	233	1
46	179	4

Table 6.1-18 reports the sizes (diameters and lengths) of the tapered proximal components used during the initial implant procedure.

Table 6.1-18. Diameters and lengths of tapered proximal component (ZTLP-PT) sizes used

Diameter (mm)	Length (mm)	n
34	161	4
	209	1
36	161	7
	209	4
38	167	1
	217	3
42	173	5
44	179	1
46	179	1

Table 6.1-19 reports the sizes (diameters and lengths) of the distal components used during the initial implant procedure.

Table 6.1-19. Diameters and lengths of distal component (ZTLP-D) sizes used

Diameter (mm)	Length (mm)	n
32	160	4
	229	1
34	142	2
	190	1
36	142	3
	190	1
38	147	4
	197	5
40	147	1
42	152	6
44	157	3
46	157	2

Table 6.1-20 reports the size (diameters and lengths) of the ancillary components used during the initial implant procedure.

Table 6.1-20. Diameters and lengths of ancillary component sizes used

Diameter (mm)	Length (mm)	n
28	108	1
32	108	2
34	112	2
36	112	1
38	91	4
42	94	3
46	97	1

Safety Results

The analysis of safety was based on the 110 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of aneurysms/ulcers of the descending thoracic aorta. Table 6.1-21 presents the results of hypothesis testing for the primary safety endpoint (30-day freedom from MAEs). MAEs were defined as the following: all-cause death; Q-wave myocardial infarction; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

Table 6.1-21. Results from primary safety hypothesis testing (MAE endpoint)

Performance Goal	30-day Freedom from MAE Rate	*P*-value	95% Confidence Interval	Performance Goal Met
80.6%	96.4% (106/110)	< 0.001	(91%, 99%)	Yes

The 30-day freedom from MAE rate was 96.4% for the present study, which met the performance goal of 80.6% ($p < 0.001$). Four patients experienced MAEs: 1 patient had a stroke (1040045), 2 patients required ventilation > 72 hours/reintubation (1030062, 1030041), and 1 patient had a stroke and required ventilation > 72 hours/reintubation (1040069).

Death, Rupture, Conversion and MAE

Table 6.1-22 provides the results from Kaplan-Meier analysis for freedom from death (all-cause and TAA-related), rupture, conversion and MAEs through 2 years. Aneurysm-related mortality was defined as death occurring within 30 days of the initial implant procedure or a secondary intervention, or any death adjudicated to be aneurysm-related by the CEC. There has been one TAA-related death (1040069) that occurred at 253 days post-procedure due to aspiration pneumonia, which the CEC had indicated was likely related to the severely debilitating stroke that the patient had suffered on the same day as the procedure. There has been one conversion to open surgical repair (1040073), which occurred at 330 days post-procedure due to aortoesophageal fistula.

Table 6.1-22. Kaplan-Meier estimates freedom from death (all-cause and TAA-related), rupture, conversion, and MAEs

Event	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
All-cause mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	2	1	3	4	1	5	11	1	12
	Cumulative censored[c]	1	0	1	2	0	2	6	1	7	10	1	11
	KM estimate[d]	1.000	1.000	1.000	0.977	0.950	0.972	0.954	0.950	0.953	0.869	0.950	0.884
	Standard error	0.000	0.000	0.000	0.016	0.049	0.016	0.023	0.049	0.020	0.037	0.049	0.032
TAA-related mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[e]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
Rupture	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	0	0	0	0	0	0
	Cumulative censored[c]	1	0	1	4	1	5	10	2	12	21	2	23
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Conversion	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[f]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
MAE[g]	Number at risk[a]	85	20	105	81	19	100	74	18	92	60	18	78
	Cumulative events[b]	4	0	4	7	1	8	12	1	13	24	1	25
	Cumulative censored[c]	1	0	1	2	0	2	4	1	5	6	1	7
	KM estimate[d]	0.956	1.000	0.964	0.922	0.950	0.927	0.864	0.950	0.879	0.722	0.950	0.763
	Standard error	0.022	0.000	0.018	0.029	0.049	0.025	0.037	0.049	0.032	0.049	0.049	0.042

[a]Number of patients at risk at the beginning of the interval.
[b]Total events up to and including the specific interval represents all patients who have had the event. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events in each category.
[c]Total censored patients up to and including the specific interval represents all patients who have met a study exit criteria or for whom data are not available at the specific interval.
[d]At end of interval.
[e]Death due to aspiration pneumonia (1040069).
[f]Conversion due to aortoesophageal fistula, adjudicated by the CEC as procedure-related (1040073).

[g]MAEs were defined as the following: all-cause death; Q-wave myocardial infarction; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

All Adverse Events

Table 6.1-23 presents the Kaplan-Meier estimates for freedom from adverse events according to organ system category.

Table 6.1-23. Kaplan-Meier estimates (freedom from morbidity, by category)

Category	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Access site/incision[a]	Number at risk[i]	84	19	103	78	18	96	72	17	89	62	17	79
	Cumulative events[j]	5	1	6	8	1	9	8	1	9	8	1	9
	Cumulative censored[k]	1	0	1	4	1	5	10	2	12	20	2	22
	KM estimate[l]	0.944	0.950	0.945	0.910	0.950	0.917	0.910	0.950	0.917	0.910	0.950	0.917
	Standard error	0.024	0.049	0.022	0.030	0.049	0.026	0.030	0.049	0.026	0.030	0.049	0.026
Cardiovascular[b]	Number at risk[i]	84	20	104	82	19	101	74	18	92	63	18	81
	Cumulative events[j]	5	0	5	5	0	5	7	0	7	8	0	8
	Cumulative censored[k]	1	0	1	3	1	4	9	2	11	19	2	21
	KM estimate[l]	0.944	1.000	0.955	0.944	1.000	0.955	0.921	1.000	0.935	0.907	1.000	0.924
	Standard error	0.024	0.000	0.020	0.024	0.000	0.020	0.029	0.000	0.024	0.032	0.000	0.026

Category	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Cerebrovascular/ neurological[c]	Number at risk[i]	86	20	106	83	19	102	76	18	94	66	18	84
	Cumulative events[j]	3	0	3	4	0	4	6	0	6	6	0	6
	Cumulative censored[k]	1	0	1	3	1	4	8	2	10	18	2	20
	KM estimate[l]	0.967	1.000	0.973	0.955	1.000	0.963	0.931	1.000	0.943	0.931	1.000	0.943
	Standard error	0.019	0.000	0.016	0.022	0.000	0.018	0.027	0.000	0.022	0.027	0.000	0.022
Gastrointestinal[d]	Number at risk[i]	88	19	107	81	18	99	76	17	93	66	17	83
	Cumulative events[j]	1	1	2	5	2	7	6	2	8	8	2	10
	Cumulative censored[k]	1	0	1	4	0	4	8	1	9	16	1	17
	KM estimate[l]	0.989	0.950	0.982	0.943	0.900	0.935	0.931	0.900	0.926	0.906	0.900	0.905
	Standard error	0.011	0.049	0.013	0.025	0.067	0.024	0.027	0.067	0.025	0.032	0.067	0.029
Pulmonary[e]	Number at risk[i]	85	20	105	81	19	100	74	18	92	66	18	84
	Cumulative events[j]	4	0	4	5	0	5	6	0	6	8	0	8
	Cumulative censored[k]	1	0	1	4	1	5	10	2	12	16	2	18
	KM estimate[l]	0.955	1.000	0.964	0.944	1.000	0.954	0.931	1.000	0.944	0.905	1.000	0.923
	Standard error	0.022	0.000	0.018	0.024	0.000	0.020	0.027	0.000	0.022	0.032	0.000	0.026
Renal[f]	Number at risk[i]	86	20	106	79	19	98	73	18	91	64	18	82
	Cumulative events[j]	3	0	3	7	0	7	10	0	10	12	0	12
	Cumulative censored[k]	1	0	1	4	1	5	7	2	9	14	2	16
	KM estimate[l]	0.967	1.000	0.973	0.921	1.000	0.935	0.885	1.000	0.905	0.859	1.000	0.855
	Standard error	0.019	0.000	0.16	0.029	0.000	0.024	0.034	0.000	0.029	0.038	0.000	0.031
Vascular[g]	Number at risk[i]	85	20	105	80	18	98	71	17	88	55	16	71
	Cumulative events[j]	4	0	4	6	1	7	10	1	11	18	2	20
	Cumulative censored[k]	1	0	1	4	1	5	9	2	11	17	2	19
	KM estimate[l]	0.955	1.000	0.963	0.933	0.950	0.936	0.884	0.950	0.896	0.789	0.894	0.801
	Standard error	0.022	0.000	0.018	0.027	0.049	0.024	0.035	0.049	0.030	0.046	0.071	0.040
Miscellaneous/ other[h]	Number at risk[i]	59	13	72	43	10	53	33	9	42	26	9	35
	Cumulative events[j]	28	7	35	44	10	54	54	10	64	61	10	71
	Cumulative censored[k]	1	0	1	1	0	1	1	1	2	1	1	2
	KM estimate[l]	0.681	0.650	0.675	0.497	0.500	0.497	0.381	0.500	0.402	0.300	0.500	0.335
	Standard error	0.050	0.107	0.045	0.054	0.122	0.048	0.052	0.122	0.048	0.049	0.112	0.046

[a]Access site/incision events included: hematoma (n=5), hernia (n=1), infection (n=2), lymph fistula (n=0), pseudoaneurysm (n=0), seroma (n=1), and wound complication requiring return to operating room (n=0).

[b]Cardiovascular events included: cardiac arrhythmia (n=4), cardiac arrest (n=0), cardiac ischemia (n=1), congestive heart failure (n=1), myocardial infarction (n=3), and refractory hypertension (n=0).

[c]Cerebrovascular/neurological events included: paralysis (n=0), paraplegia (n=0), paraparesis > 30 days (n=1), spinal cord shock (n=0), transient ischemic attack (n=0), and stroke (n=5).
[d]Gastrointestinal events included: bleeding (n=4), bowel ischemia (n=2), infection (n=4), mesenteric ischemia (n=1), and paralytic ileus > 4 days (n=0).
[e]Pulmonary events included: COPD (n=1), hemothorax (n=0), pleural effusion (n=1), pneumonia (n=6), pneumothorax (n=0), pulmonary edema (n=0), pulmonary embolism (n=1), and pulmonary embolism involving hemodynamic instability or surgery (n=0).
[f]Renal events included: renal failure (n=4), UTI (n=6), serum creatinine rise > 30% above baseline resulting in a persistent value > 2.0 mg/dl (n=2).
[g]Vascular events included: aneurysm (n=11), aortobronchial fistula (n=1), aortoesophageal fistula (n=1), aortoenteric fistula (n=0), coagulopathy (n=1), deep vein thrombosis (n=0), dissection (n=3), embolism (n=2), hematoma (n=1), pseudoaneurysm (n=1), thrombosis (n=1), and vascular injury (n=5).
[h]Miscellaneous/other events included: hypersensitivity/allergic reaction (n=1), multi-organ failure (n=2), sepsis (n=2), and other (n=70).
[i]Number of patients at risk at the beginning of the interval.
[j]Total events up to and including the specific interval represents all patients who have had the event. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events in each category.
[k]Total censored patients up to and including the specific interval represents all patients who have met a study exit criteria or for whom data are not available at the specific interval.
[l]At end of interval.

Effectiveness Results

Table 6.1-24 presents the results of hypothesis testing for the primary effectiveness endpoint (12-month device success) for the Zenith Alpha™ Thoracic Endovascular Graft.

Table 6.1-24. Results from primary effectiveness hypothesis testing (device success endpoint)

Performance Goal	12-month Device Success Rate	*P*-value	95% Confidence Interval	Performance Goal Met
80.7%	92.7% (102/110)[a]	< 0.001	(86.2%, 96.8%)	Yes

[a]The performance goal was originally calculated with a 365-day cutoff for inclusion of events (e.g., secondary interventions) and the results in the present study were analyzed in the same fashion for consistency such that the 12-month device success rate was 95.5% (105/110) with a 95% confidence interval of 89.7%, 98.5%. However, there were 3 additional patients in the present study who had an endoleak detected at the 12-month follow-up and subsequently underwent secondary intervention > 365 days after the index procedure; therefore, a conservative analysis was performed that included these 3 additional patients as failures (as shown in the table).

The 12-month device success rate was 92.7% for the present study (using the conservative analysis shown in Table 6.1-24), which met the performance goal of 80.7% ($p < 0.001$). There were 5 patients who did not meet the effectiveness endpoint of 12-month device success (using the original 365-day cutoff for events), as follows. Two patients (1030014, 1030098) did not receive the device due to an inability to insert/advance the introduction system and were therefore technical failures. In patient 1030014 (87-year-old white female), the introduction system became lodged at the aortic bifurcation in the right common iliac artery despite attempts to increase the diameter of the iliac artery. In patient 1030098 (73-year-old white female), the index procedure was aborted due to difficulty inserting a dilator in the left limb of a previous aneurysm repair; the previous endovascular abdominal aortic aneurysm repair made the patient a poor candidate for a conduit. Three patients (1030017, 1030046, 1040073) experienced aneurysm growth greater than 5 mm at the 12-month follow-up, one of whom (1040073) also underwent conversion to open surgical repair 330 days post-procedure due to an aortoesophageal fistula. There were 3 additional patients who had endoleak detected at 12-month follow-up and subsequently underwent secondary intervention > 365 days after the index procedure (1030047, 1030072, 1030095). Sensitivity to missing data, including a worst-case analysis, was performed, and met the performance goal.

Device Performance

Table 6.1-25 presents changes in aneurysm size, as observed from the 30-day (baseline) measurement to each follow-up exam through 2 years (based on core laboratory evaluation). A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Aneurysm growth was associated with detectable endoleak in six patients, four of whom underwent secondary intervention. There was no detectable endoleak in the remaining five patients with aneurysm growth, two of whom had no change in aneurysm size (≤ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak, two required secondary intervention and one had growth at the last available follow-up; each growth was associated with an inadequate seal zone length (i.e., length < 20 mm) as well as graft undersizing. Each patient who had growth that did not resolve spontaneously or was not associated with a Type II endoleak was initially treated for an aneurysm using only a proximal component, underscoring the importance of adhering to the sizing guidelines in the Instructions for Use (IFU), both in terms of component diameter as well as component type and length, which includes the use of a two-component repair (proximal and distal component) when treating aneurysms.

Table 6.1-25. Change in aneurysm diameter/ulcer depth based on results from core laboratory analysis

Item	Percent Patients (number/total number)								
	Aneurysm			Ulcer			All		
	6-month	12-month	2-years	6-month	12-month	2-years	6-month	12-month	2-years
Increase (> 5 mm)	4.2% (3/72) [a,b,c]	4.2% (3/71) [a,c,d]	14.8% (9/61)[a,d,e-k]	0	0	0	3.3% (3/90)	3.4% (3/88)	12.0% (9/75)
Decrease (> 5 mm)	19.4% (14/72)	31.0% (22/71)	24.6% (15/61)	33.3% (6/18)	52.9% (9/17)	64.3% (9/14)	22.2% (20/90)	35.2% (31/88)	32.0% (24/75)
No change (≤ 5 mm)	76.4% (55/72)	64.8% (46/71)	60.7% (37/61)	66.7% (12/18)	47.1% (8/17)	35.7% (5/14)	74.4% (67/90)	61.4% (54/88)	56.0% (42/75)

Note: the number of patients with adequate imaging to assess for size increase reflects the number of exams in which aneurysm diameter/ulcer depth was able to be assessed at each specified time point, whereas the denominators in this table also take into account the availability of a baseline exam to which to compare.

[a]Patient 1030046 – The patient was treated at the time of the index procedure with a single proximal component. The patient underwent a secondary intervention prior to the 2-year follow-up (Table 6.1-30) to treat the unexplained aneurysm growth (i.e., no detectable endoleaks). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a proximal seal length < 20 mm.

[b]Patient 1040060 – The patient has not required a secondary intervention. Per core laboratory evaluation, no endoleaks have been identified in this patient. Aneurysm size was stable at 12 months (< 5 mm increase).

[c]Patient 1040073 – The patient had a Type IIb endoleak, which was treated prior to the 12-month follow-up (Table 6.1-30).

[d]Patient 1030017 – The patient was treated at the time of the index procedure with a single proximal component. The patient had no evidence of detectable endoleak. The patient underwent a secondary intervention beyond 2 years (placement of a distal component 922 days post-procedure for aneurysm growth). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.
[e]Patient 1040034 – The patient has not had a secondary intervention and core laboratory results indicate no growth at 3 years.
[f]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had distal Type I endoleak (Table 6.1-26) and CEC-confirmed migration (Table 6.1-27). A secondary intervention was performed (ancillary component placement) on post-operative day 727 (Table 6.1-30) and no growth was noted at 3-years. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm.
[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was also noted at the 2-year follow-up (Table 6.1-26). The patient underwent a secondary intervention beyond 2 years (ancillary component placement 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing.
[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. Per core laboratory evaluation, a Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak (Table 6.1-26) has been identified in the patient at 2 years (previous endoleaks identified were Type II). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.
[i]Patient 1040041 – The patient was treated at the time of the index procedure with a single proximal component. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient withdrew from the study 906 days post-procedure.
[j]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had a distal Type I endoleak (Table 6.1-26) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing.
[k]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month and 2-year follow-ups (Table 6.1-26). A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. No secondary interventions have been performed to date. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm.

Endoleaks classified by type, as assessed by the core laboratory at each exam period through 2 years, are reported in Table 6.1-26. In total, there were seven patients found to have a Type I (distal) endoleak and two patients found to have a Type III (nonjunctional) endoleak at one or more time points, two of which (one with Type I and one with Type III) had no evidence of the same endoleak at last available follow-up and without the patients having undergone secondary intervention. Endoleak in the other seven patients (five of which required secondary intervention) was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing, which occurred following aneurysm treatment with only a proximal component in six of the patients, underscoring the

importance of adhering to the sizing guidelines in the IFU, both in terms of component diameter as well as component type and length, including the use of a two-component repair (proximal and distal components) when treating aneurysms.

Table 6.1-26. Endoleak based on results from core laboratory analysis

Type	Percent Patients (number/total number)											
	1-month			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Any (new only)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	4.1% (3/73)	5.6% (1/18)	4.4% (4/91)	4.5% (3/66)	0	3.6% (3/83)	8.5% (5/59)	0	6.8% (5/73)
Any (new and persistent)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	11.0% (8/73)	11.1% (2/18)	11.0% (10/91)	10.6% (7/66)	0	8.4% (7/83)	16.9% (10/59)	0	13.7% (10/73)
Multiple	2.4% (2/82)[a]	0	2.0% (2/102)	2.7% (2/73)[a]	0	2.2% (2/91)	1.5% (1/66)	0	1.2% (1/83)	0	0	0
Proximal Type I	0	0	0	0	0	0	0	0	0	0	0	0
Distal Type I	2.4% (2/82)[a,b]	0	2.0% (2/102)	4.1% (3/73)[a,b,d]	0	3.3% (3/91)	4.5% (3/66)[b,d,e]	0	3.6% (3/83)	8.5% (5/59)[b,e,g-i]	0	6.8% (5/73)
Type II	7.3% (6/82)[a]	0	5.9% (6/102)	9.6% (7/73)[a,b]	5.6% (1/18)	8.8% (8/91)	6.1% (4/66)[b]	0	4.8% (4/83)	6.8% (4/59)	0	5.5% (4/73)
Type III	0	5.0% (1/20)[c]	1.0% (1/102)	0	5.6% (1/18)[c]	1.1% (1/91)	1.5% (1/66)[f]	0	1.2% (1/83)	0	0	0
Type IV	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	1.2% (1/82)	5.0% (1/20)	2.0% (2/102)	0	0	0	0	0	0	1.7% (1/59)	0	1.4% (1/73)

[a]Patient 0463776 – Distal Type I and Type IIb endoleaks were noted at the 1- and 6-month follow-ups. The endoleak type was noted as unknown at last follow-up (unscheduled follow-up at day 300); a decrease in aneurysm size was also noted at last follow-up. No secondary interventions have been performed to date and the patient has since withdrawn from the study.

[b]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month and 2-year follow-ups. A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. The patient also had aneurysm growth (Table 6.1-25). No secondary interventions have been performed to date. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm.

[c]Patient 1040051 – The Type III (nonjunctional) endoleak noted at the 1-month and 6-month follow-ups was no longer present at the 12-month follow-up. The location of the endoleak coincided with an area of prominent calcification in the aorta. No secondary interventions have been performed to date and the patient has not demonstrated an increase in aneurysm size.

[d]Patient 1030072 – A distal Type I endoleak was noted at the 6-month and 12-month follow-ups. A secondary intervention has occurred (for the site-reported reason of distal Type I endoleak after 12-month follow-up). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient underwent a secondary intervention on post-operative day 420 (Table 6.1-30) and there was no endoleak detected at the 2-year follow-up.

[e]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted at the 12-month follow-up (and again at an unscheduled CT (596 days post procedure)) and the 2-year follow-up, at which time the patient underwent secondary intervention. The patient also had aneurysm growth (Table 6.1-25) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention (ancillary component placement) 727 days post-procedure (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. There was no endoleak detected at the 3-year follow-up.

[f]Patient 1030095 – The patient was treated at the time of the index procedure with a single proximal component. A Type III (nonjunctional) endoleak was noted at the 12-month follow-up (a secondary intervention involving distal component placement was performed after the 12-month follow-up for the site-reported reason of distal Type I endoleak; Table 6.1-30). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) in combination with the site-reported reason for secondary intervention (distal Type I, not Type III, endoleak) suggest graft undersizing. Patient has subsequently withdrawn from the study on post-operative day 695.

[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25) and underwent a secondary intervention beyond 2 years (ancillary component placement 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing.

[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. Per core laboratory evaluation, a Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak has been identified in the patient at 2 years (previous endoleaks identified were Type II). The patient also had aneurysm growth (Table 6.1-25). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.

[i]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had aneurysm growth (Table 6.1- 25) and CEC-confirmed migration (Table 6.1-27) and underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing.

The results for migration through 2 years, as confirmed by the CEC, are provided in Table 6.1-27. There were three cases of CEC-confirmed migration (two also with aneurysm growth, distal Type I endoleak, and the need for secondary intervention), each of which was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing and occurred following aneurysm treatment with only a proximal component, underscoring the importance of adhering to the sizing guidelines in the IFU, both in terms of component diameter as well as component type and length, including the use of a two-component repair (proximal and distal components) when treating aneurysms.

Table 6.1-27. Percent of patients (aneurysm and ulcer) with CEC-confirmed migration (date of first occurrence)

Item	Percent Patients (number/total number)		
	6-month	12-month	2-year
Migration (> 10 mm)	0% (0/94)	0% (0/92)	3.9% (3/77)[a,b,c]

[a]Patient 1030012 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. There was no evidence of endoleak, and the aneurysm size has continuously decreased from 61 mm at 1 month to 40 mm at 2 years and 38 mm at 3 years. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.

[b]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had aneurysm growth (Table 6.1-25), distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.

[c]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had aneurysm growth (Table 6.1-25), a distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing

The results from core laboratory analysis for graft kink/compression through 2 years are summarized in Table 6.1-28.

Table 6.1-28. Core laboratory reports of graft kink/compression

Item	30-day	6-month	12-month	2-year
Kink/compression	0	0	0	1.3% (1/77)[a]

[a]Patient 0468761 – The patient had a kink in the proximal and distal components identified by the core laboratory on the 2-year CT scan. There were no clinical sequelae associated with the kink; at the 2-year follow-up, the aneurysm had decreased in size and the device was patent. The patient died prior to the next follow-up visit.

CEC-confirmed device integrity observations at each exam period through 2 years are summarized in Table 6.1-29.

Table 6.1-29. CEC-confirmed loss of device integrity

Finding	Percent Patients (number/total number)											
	30-day			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Barb separation	0	0	0	0	0	0	0	0	0	0	0	0
Stent fracture	1.2% (1/85)[a]	0	1.0% (1/105)	1.3% (1/80)[a]	0	1.0% (1/98)	1.3% (1/75)[a]	0	1.1% (1/92)	1.6% (1/63)[a]	0	1.3% (1/77)
Component separation	0	0	0	0	0	0	0	0	0	0	0	0

[a]Patient 1030069 – Patient had a report of a single stent fracture (of the second covered stent in the proximal device) seen on the 30-day, 6-month, 12-month and 2-year x-rays. Nothing uncharacteristic regarding the anatomy or deployment of the graft was observed. This patient has had no clinical sequelae from the stent fracture.

Tables 6.1-30 and 6.1-31 summarize the site-reported reasons for secondary intervention and types of secondary intervention, respectively.

Table 6.1-30. Site-reported reasons for secondary intervention (all patients)

Reason	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Device migration	0	0	0	1[g]
Endoleak				
Type I proximal	0	0	0	0
Type I distal	0	0	0	3[d,g,h]
Type II	0	0	1[b]	0
Type III (graft overlap joint)	0	0	0	0
Type III (hole/tear in graft)	0	0	0	0
Type IV (through graft body)	0	0	0	1[i]
Unknown	0	0	0	0
Other	1[a]	0	1[c]	2[e,f]

[a]Patient 1040058 (ulcer) – Patient had pre-planned left subclavian artery embolization and right-to-left subclavian artery bypass 7 days after the index procedure.
[b]Patient 1040073 (aneurysm) – Patient had two separate secondary interventions for Type II endoleak: unsuccessful attempt at placing embolization coils in the intercostal artery, followed by successful direct puncture of the aneurysm with delivery of N-butyl cyanoacrylate.
[c]Patient 1040037 (aneurysm) – Patient had additional component placed for aortic dissection proximal to the study device 324 days after the index procedure.
[d]Patient 1030072 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal components and balloon angioplasty 420 days after the index procedure.
[e]Patient 0467042 (aneurysm) – Patient had a dissection distal to the most distal stent. Ancillary components were placed 433 days after the index procedure.
[f]Patient 1030046 (aneurysm) – Patient had observed progression of disease treated with additional proximal and distal components 594 days after the index procedure.
[g]Patient 1030047 (aneurysm) – Patient had observed device migration and Type I distal endoleak treated with ancillary components 727 days after the index procedure.
[h]Patient 1030095 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal components 534 days after the index procedure.
[i]Patient 1040054 (aneurysm) – Patient had persistent Type IV endoleak per site analysis (unknown type endoleak per core laboratory analysis) treated with ancillary components 599 days after the index procedure.

Table 6.1-31. Types of secondary interventions

Type*	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Percutaneous				
Ancillary component placed	0	0	1[b]	6[d-i]
Balloon angioplasty	0	0	0	1[d]
Coil embolization	0	0	0	0
Stent	0	0	0	0
Thrombectomy	0	0	0	0
Thrombolysis	0	0	0	0
Other	0	0	1[b]	0

Type*	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Surgical				
Conversion to open repair	0	0	0	0
Surgical bypass procedure	0	0	0	0
Other	1[a]	0	0	0
Other	0	0	1[c]	0

*A patient may have had more than one treatment type.
[a-i]Refer to the footnotes in Table 6.1-30 for additional details.

Gender Subset Analysis

There was nearly an equal proportion of males (n = 64, 58.2%) and females (n = 46, 41.8%) enrolled in this study, allowing for further analysis of outcomes by gender. There was no significant difference in age between male (70.7 ± 9.9 years; 42 – 85 years) and female (74.3 ± 9.4 years; 44 – 92 years) patients. Furthermore, the access method used (cutdown vs. percutaneous vs. conduit) was not significantly different between male (56.3% cutdown, 43.8% percutaneous, 0% conduit) and female (71.7% cutdown, 26.1% percutaneous, 2.2% conduit) patients.

No significant differences between males and females with respect to primary safety and effectiveness endpoints were found. For the primary safety endpoint, the 30-day freedom from MAE rate was 96.9% (62/64) for males and 95.7% (44/46) for females. For the primary effectiveness endpoint, the 12-month device success rate was 96.9% (62/64) for males and 93.5% (43/46) for females. Overall, males and females treated with the Zenith Alpha™ Thoracic Endovascular Graft had similar outcomes, indicating the device is likely to be equally safe and effective for both males and females.

Summary

All but 2 patients received at least one proximal component, and approximately one-third of patients also received a distal component (i.e., a two-piece system), as compared to approximately two-thirds of patients in the previous study who were treated with a two-piece system. Therefore, a two-component repair was less often used in this study compared to the previous study, despite similar percentages of patients from both studies having been treated for aneurysms. The IFU for the Zenith Alpha™ Thoracic Endovascular Graft was therefore updated to emphasize the importance of a two-component repair when treating aneurysms given that the reports of growth, migration, and distal Type I endoleak tended to occur in only aneurysm patients who were treated using a single proximal component.

Two patients did not receive a device in this study due to an inability to advance/gain access to the target treatment site; 2 patients also did not receive a device in the previous study for similar reasons. In patients where access was gained (n = 108), all devices were deployed successfully in the intended location and all vessels were patent at the time of deployment. An access conduit was necessary for graft delivery in 0.9% of patients, and percutaneous access was used in 36% of patients.

There were no deaths within 30 days of endovascular repair. There was one TAA-related death within 365 days, resulting in a 99% freedom from TAA-related mortality at 1 year. There were no ruptures reported at any follow-up time period. One patient underwent conversion to open repair 330 days post-procedure due to an aortoesophageal fistula; the CEC adjudicated the event as related to the procedure. The patient survived the surgical repair and investigational device explant and has since exited the study. Patients experienced adverse events in each of the organ system categories.

A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Aneurysm growth was associated with detectable endoleak in six patients, four of whom underwent secondary intervention. There was no detectable endoleak in the remaining five patients with aneurysm growth, two of whom had no change in aneurysm size ($\leq$ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak, two required secondary intervention and one had growth at the last available follow-up; each growth was associated with an inadequate seal zone length (i.e., length < 20 mm) as well as graft undersizing.

The majority of endoleaks detected were Type II, and there were no proximal Type I or Type IV endoleaks at 24 months. In total, there were seven patients found to have a Type I (distal) endoleak and two patients found to have a Type III (nonjunctional) endoleak at one or more time points, two of which (one with Type I and one with Type III) had no evidence of the same endoleak at last available follow-up and without the patients having undergone secondary intervention. Endoleak in the other seven patients (five of which required secondary intervention) was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing.

There were three cases of CEC-confirmed migration (two also with aneurysm growth, distal Type I endoleak, and the need for secondary intervention), each of which was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft

undersizing. There was one report of loss of device integrity (a single stent fracture) within 24 months, but with no adverse clinical sequelae.

In total, nine patients required a secondary intervention within 24 months for the site reported reasons of left subclavian artery embolization with bypass (n=1), Type II endoleak (n=1), distal Type I endoleak (n=2), distal Type I endoleak and migration (n=1), Type IV endoleak (n=1), disease progression (n=1), and aortic dissection (n=2).

Both the safety (30-day freedom from MAEs) and effectiveness (12-month device success) hypotheses were met. Overall, the results provide a reasonable assurance of the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft.

6.2. Clinical Study for the BTAI Indication

The Zenith Alpha™ Thoracic Endovascular Graft clinical study is a prospective, nonrandomized, noncomparative, single-arm, multicenter study that was conducted to evaluate the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with BTAI. Enrollment in the clinical trial began on January 23, 2013 and was completed May 7, 2014. Seventeen US institutions enrolled a total of 50 patients in the study for the BTAI indication under IDE G120085. The data presented herein were collected through April 1, 2015.

The Zenith Alpha™ Thoracic Endovascular Graft for BTAI study had two endpoints. The primary safety endpoint was all-cause and aortic-injury-related mortality at 30 days, the latter of which was defined as any death determined by the independent CEC to be causally related to the initial implant procedure, secondary intervention, or rupture of the transected aorta. The primary effectiveness endpoint was device success at 30 days, which was defined as successful access of the injury site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location with patency at the time of deployment completion (technical success) plus none of the following at 30 days: device collapse, Type I or III endoleak requiring reintervention, or conversion to open surgical repair. All data were analyzed using descriptive statistics. Data were not analyzed for the purpose of statistical inference, as BTAI patients typically have extensive concomitant injuries that would confound the interpretation of statistical comparisons to alternative treatments.

An independent core laboratory analyzed all patient imaging. An independent CEC adjudicated relevant adverse events, including all patient deaths. An independent DSMB monitored the clinical trial according to an established safety monitoring plan.

The study follow-up schedule (Table 6.2-1) consisted of imaging (CT) and clinical assessments at post-procedure (clinical assessment only at pre-discharge), 30 days, 6 months, 12 months, and yearly thereafter through 5 years.

Table 6.2-1. Study follow-up schedule

	Pre-op	Intra-op	Post-procedure	30-day	6-month	12-month[c]
Clinical exam	X		X	X	X	X
Blood tests	X		X			
CTA	X[a]			X[b]	X[b]	X[b]
Angiography		X				

[a]The CTA must be obtained as close as possible to the study procedure.

[b]MR or noncontrast CT imaging may be used for those patients experiencing renal failure or who are otherwise unable to undergo contrast-enhanced CT scan, with TEE being an additional option in the event of suboptimal MR imaging.
[c]Performed yearly for 5 years.

Although the primary safety and effectiveness endpoints were evaluated at 30 days, patient data presented herein include longer-term follow-up that was available at the time of the data lock (April 1, 2015). Table 6.2-2 reports the percent of follow-up data available through 24 months.

Table 6.2-2. Follow-up availability

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]			Events Occurring Before Next Interval			
		Clinical	CT[c]	ND	Endoleak	Migration	Aortic Injury Healing	Death	Conversion to Open Repair	Lost to Follow-up/ Withdrawal	Not Due for Next Visit
Operative	50	50/50 (100%)	NA	0	NA	NA	NA	0[d]	0	0	0
30-day	50[d]	46/50 (92.0%)	43/50 (86.0%)	0	42/50 (84.0%)	10/50 (20.0%)[f]	42/50 (84.0%)	5[d]	0	4	0
6-month	41	32/41 (78.0%)	34/41 (82.9%)	0	34/41 (82.9%)	33/41 (80.5%)	34/41 (82.9%)	0	1	1	0
12-month	39	26/39 (66.7%)	26/39 (66.7%)	11	25/39 (64.1%)	20/39 (51.3%)	25/39 (64.1%)	0	0	2	32
24-month	5	0.0% (0/5)	0.0% (0/5)	5	0.0% (0/5)	0.0% (0/5)	0.0% (0/5)	0	0	0	5

ND – Visit not done, but patient still eligible for follow-up.
NA – Not assessed.
[a]Site-submitted data.
[b]Based on core laboratory analysis – Does not include imaging exams received by the core laboratory for analysis, but that have not yet been analyzed.
[c]Includes MRI or TEE imaging (which is allowed per protocol) when a patient is unable to receive contrast medium due to renal failure.
[d]Patient 1200054 – The patient underwent 30-day follow-up (CT scan and clinical exam) 22 days post-procedure before exiting the study due to death 24 days post-procedure.
[e]As the 30-day time point represented the baseline CT for migration assessments, the core laboratory only assessed 30-day migration for 10 patients, who had an unscheduled post-procedure CT scan that was used as the baseline scan.

Demographics and Patient Characteristics

The demographics and patient characteristics are presented in Table 6.2-3. Height and weight measurements were not assessed.

Table 6.2-3. Demographics and patient characteristics

Demographic	Mean ± SD (n, range) or Percent Patients (number/total number)
Age (years)	
All patients	42.7 ± 18.7 (n=50, 18 – 89)
Male	42.3 ± 19.6 (n=44, 18 – 89)
Female	45.5 ± 11.0 (n=6, 28 – 59)
Gender	
Male	88.0% (44/50)
Female	12.0% (6/50)
Ethnicity	
White	76.0% (38/50)
Hispanic or Latino	10.0% (5/50)
Black or African American	8.0% (4/50)
American Indian or Alaska Native	0
Asian	6.0% (3/50)
First Nations	0

The medical history and comorbid medical conditions for the patient cohort are presented in Table 6.2-4.

Table 6.2-4. Pre-existing comorbid medical conditions

Medical History	Percent Patients (number/total number)[a]
Cardiovascular	
Cardiac arrhythmia	2.0% (1/50)
Congestive heart failure (CHF)	0
Coronary artery disease	6.0% (3/50)
Myocardial infarction (MI)	4.0% (2/50)
Surgical or percutaneous treatment	6.0% (3/50)
Vascular	
Thromboembolic event	0
Peripheral vascular disease	0
Aneurysm (patient history)	0
Dissection	0
Bleeding diathesis or uncorrectable coagulopathy	0
Carotid endarterectomy	0
Hypertension	26.0% (13/50)
Pulmonary	
Chronic obstructive pulmonary disease (COPD)	2.0% (1/50)
Renal	
Chronic renal insufficiency	0
Dialysis	0
Endocrine	
Diabetes	10.0% (5/50)

Medical History	Percent Patients (number/total number)[a]
Infectious disease	
Sepsis	0
Hepatobiliary	
Liver disease	4.0% (2/50)
Neoplasms	
Cancer	6.0% (3/50)
Neurologic	
Paralysis	0
Paraparesis	0
Stroke	0
Transient ischemic attack/reversible ischemic neurologic deficit	0
Connective tissue	
Marfan Syndrome	0
Ehlers Danlos	0
Substance use	
Past or current smoker	46.0% (23/50)

Assessments of pre-procedure risk (ASA classification, Glasgow coma scale, and injury severity score) are presented in Table 6.2-5.

Table 6.2-5. Pre-procedure risk

Measure	Percent Patients (number/total number) or Mean ± SD or Median (n, range)
ASA classification	
1	0
2	8.0% (4/50)
3	26.0% (13/50)
4	50.0% (25/50)
5	16.0% (8/50)
Glasgow coma scale (GCS)	
Mild ≥ 13	48.0% (24/50)
Moderate 9 – 12	18.0% (9/50)
Severe ≤ 8	34.0% (17/50)
Injury severity score (ISS)	
Mean	31.0 ± 14.0 (n=50, 3 – 66)
Median	29.0 (n=50, 3 – 66)

Concomitant injuries are presented in Table 6.2-6.

Table 6.2-6. Concomitant injuries

Injury	Percent Patients (number/total number)
Abdominal injuries (solid organ, bowel, bladder)	62.0% (31/50)
Head injury	40.0% (20/50)
Long bone fracture	58.0% (29/50)
Lung injury	60.0% (30/50)
Neurological deficits	18.0% (9/50)

Injury	Percent Patients (number/total number)
Pelvis fracture	30.0% (15/50)
Rib fractures	72.0% (36/50)
Scapula fracture	12.0% (6/50)
Unstable fractures (cervical/thoracic/lumbar spine)	14.0% (7/50)
Other[a]	34.0% (17/50)

[a]Other concomitant injuries as reported by the sites include: open fracture right tibia and fibula, left knee traumatic arthrotomy, right radial and ulnar fractures, C6-C7 abnormality (widening of space), grade 11B left ICA dissection at C2 level, open dislocation of ankle, closed fracture of distal phalanx or phalanges (thumb), open scalp wound, open pubis fracture, closed fracture of the nasal bones, closed fracture of pubis, closed fracture of shaft of the tibia, fracture of navicular (scaphoid) bone of foot, respiratory distress syndrome, pneumonia, clavicle fracture, right external ventricular drain placement, small hemorrhagic left pleural effusion, small left pneumothorax, right first metatarsal fracture, right orbital floor fracture, right maxillary sinus fractures, facial fractures, severed left lower extremity, bruising on the abdomen, left hip contusion, right and left knee abrasions, history of seizure disorder, and bilateral nasal bone fracture.

The etiology of thoracic aortic injury for the patients enrolled in the study is presented in Table 6.2-7.

Table 6.2-7. Etiology of the thoracic injury

Etiology of Thoracic Injury	Percent Patients (number/total number)
Fall	4.0% (2/50)
Motor vehicle accident	72.0% (36/50)
Motorcycle accident	14.0% (7/50)
Pedestrian hit by a motor vehicle	6.0% (3/50)
Other[a]	4.0% (2/50)[a]

[a]One patient (1200070) was riding a moped and was hit by a motor vehicle. One patient (1200046) was riding a bicycle and was hit by a motor vehicle.

The results from core laboratory analysis of pre-procedure aortic injury grade are provided in Table 6.2-8.

Table 6.2-8. Pre-procedure aortic injury grade based on core laboratory analysis

Characteristic	Percent Patients (number/total number)
Traumatic aortic injury grade	
1 (intimal tear)	0
2 (intramural hematoma/large intimal flap)	8.0% (4/50)
3 (pseudoaneurysm)	86.0% (43/50)
4 (rupture)	6.0% (3/50)

Table 6.2-9 reports presenting anatomical dimensions.

Table 6.2-9. Presenting anatomical dimensions reported per the core laboratory

Measure	Mean ± SD (n, range)
Aortic injury Maximum diameter (mm) Length (mm)	 31.5 ± 6.4 (n=47, 21.3 – 48.4) 31.5 ± 18.0 (n=49, 9.8 – 118.6)
Length from left common carotid artery to most proximal extent of aortic injury (mm)	27.8 ± 13.3 (n=48, 0.1 – 73.1)
Length from celiac artery to most distal extent of aortic injury	186.0 ± 28.8 (n=41, 103.9 – 252.7)
Maximum aortic diameter in intended proximal seal zone (mm)	27.9 ± 6.0 (n=45, 19.7 – 48.2)
Maximum aortic diameter in intended distal seal zone (mm)	25.2 ± 5.9 (n=38, 16.8 – 41.3)
Right common iliac artery Narrowest segment (mm)	 6.7 ± 1.6 (n=38, 3.5 – 10.3)
Left common iliac artery Narrowest segment (mm)	 6.9 ± 1.5 (n=38, 3.9 – 9.7)

Procedural Information

The majority (98.0%) of procedures were performed under general anesthesia. Vascular access was gained via femoral artery cutdown in 56.0% of patients and percutaneously in 44.0% of patients. Adjunctive procedures to prevent paraplegia, specifically CSF drainage, were performed in 4.0% of patients, and induced hypotension for accurate deployment was used in 10.0% of patients. The LSA was covered partially or completely in 47.8% of patients. No supra-aortic vessel bypass was performed. The most common location of the aortic injury was at the isthmus in 56.0% of patients, followed by the distal descending thoracic aorta in 34.0% of patients. The mean procedure time was 85.3 ± 44.3 minutes (range 34-278 minutes) and the mean procedural blood loss was 102.5 ± 144.6 ml. The mean anesthesia time was 182.9 minutes and the mean fluoroscopy time was 8.6 ± 8.3 minutes. The access techniques used are presented in Table 6.2-10.

Table 6.2-10. Access technique used to insert the endovascular graft

Type	Percent Patients (number/total number)
Percutaneous	44.0% (22/50)[a]
Cutdown	56.0% (28/50)
Conduit	0

[a]For 2 patients, device delivery was preformed percutaneously; however, subsequent cutdown was required to close the access site due to a percutaneous closure device failure (1200075) and to treat femoral artery stenosis (1200042).

The location of the graft components relative to an identified site is provided in Table 6.2-11.

Table 6.2-11. Graft location based on core laboratory analysis

Location	Percent Patients (number/total number)
Proximal edge of graft material	
Above left common carotid artery	0
Below left common carotid artery, above left subclavian artery	47.8% (22/46)*
Below left subclavian artery	52.1% (24/46)
Distal aspect of graft	
Above celiac artery	100% (46/46)
Below celiac artery	0

*The left subclavian artery was completely covered in 7 patients and partially covered in 15 patients.

All patients survived the endovascular procedure. Technical success was achieved in all patients (100%). Overall, the procedural results were as expected for the treatment of patients with BTAI.

Clinical Utility Measures

The clinical utility results are presented in Table 6.2-12.

Table 6.2-12. Clinical utility measures

Clinical Utility	Mean ± SD (n, range)
Duration of ICU stay (days)	17.8 ± 20.1 (n=50, 1 – 126)[a]
Duration of mechanical ventilation (days)	13.4 ± 20.9 (n=50, 0 – 127)[a]
Days to resumption of oral fluid intake	10.4 ± 14.9 (n=45, 0 – 78)[b-d]
Days to resumption of regular diet	14.3 ± 18.8 (n=44, 0 – 99)[a-d]
Days to resumption of bowel function	5.8 ± 4.9 (n=46, 0 – 24)[e]
Days to hospital discharge	25.0 ± 24.3 (n=50, 2 – 125)[a]

[a]Patient 1200079 required ICU stabilization 1 day prior to the procedure (126 days total) and required mechanical ventilation for 2 days prior to the procedure (127 days total). The BTAI treatment was postposed as the patient required further resuscitation and stabilization of a left lower extremity injury. This patient has not resumed regular diet intake and is currently receiving nutrition from a percutaneous endoscopic gastrostomy (PEG) tube.
[b]Days to resumption of oral fluid intake and regular diet were not reported for patient 1200041. The patient was placed on a feeding tube until death occurred on post-operative day 36.
[c]Three patients (1200024, 1200051, and 1200057) were discharged from the hospital before resumption of oral fluid intake and regular diet occurred.
[d]Days to resumption of oral fluid intake and regular diet were unknown for 1 patient (1200074).
[e]Days to resumption of bowel function was unknown for 4 patients (1200015, 1200023, 1200041, and 1200067).

Devices Implanted

Table 6.2-13 presents the percent of patients who received one or more Zenith Alpha™ Thoracic Endovascular Graft proximal components during the implant procedure. Also reported is the range of graft diameters that were implanted. One patient (1200012) received two study components (the second component was placed to extend graft coverage distally). While all other patients received a single study component, it should be noted that one patient (1200040) received two commercial components in combination with a single study component. The first study component and first commercial component placed were the same diameter and had been undersized as measurements were taken from a pre-procedure CT scan performed while the patient was not fully resuscitated; the final component placed (second commercial component) was larger in diameter than the two previously placed components. The IFU therefore underscores that graft sizing for BTAI should be based on measurements in a fully resuscitated patient.

Table 6.2-13. Number of study components deployed and graft diameter range

Number of Components Deployed	Percent Patients (number/total number)	Graft Diameter Range
1	98.0% (49/50)[a]	18 to 38 mm
2	2.0% (1/50)[b]	

[a]Patient 1200040 received one study component and two commercial components. The first study component and first commercial component placed were the same diameter and had been undersized, as measurements were taken from a pre-procedure CT scan performed while the patient was not fully resuscitated; the final component placed (second commercial component) was larger in diameter than the two previously placed components.
[b]Patient 1200012 received two study components; the additional study component was placed to extend graft coverage distally.

Table 6.2-14 reports the specific sizes (diameters and lengths) of the nontapered proximal components used during the initial implant procedure.

Table 6.2-14. Diameters and lengths of nontapered proximal component (ZTLP-P) sizes used

Diameter (mm)	Length (mm)	n
18	105	2
20	105	1
22	105	1
24	105	11
26	105	6
28	109	4
30	109	6
32	109	3[a]
34	113	3
36	113	1

Diameter (mm)	Length (mm)	n
38	117	3

[a]Patient 1200012 received two 32 x 109 mm proximal components.

Table 6.2-15 reports the specific sizes (diameters and lengths) of the tapered proximal components used during the initial implant procedure.

Table 6.2-15. Diameters and lengths of tapered proximal component (ZTLP-PT) sizes used

Diameter (mm)	Length (mm)	n
26	105	9
30	108	1

The access technique used is presented in Table 6.2-16.

Table 6.2-16. Access technique used to insert the endovascular graft

Type	Percent Patients (number/total number)
Percutaneous	44.0% (22/50)[a]
Cutdown	56.0% (28/50)
Conduit	0

[a]For 2 patients, device delivery was preformed percutaneously; however, subsequent cutdown was required to close the access site due to a percutaneous closure device failure (1200075) and to treat femoral artery stenosis (1200042).

Safety Results

The analysis of safety was based on the 50 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of BTAI. The primary safety endpoint for the study was all-cause and aortic-injury-related mortality at 30 days. Aortic-injury-related mortality was defined as any death determined by the independent CEC to be causally related to the initial implant procedure, secondary intervention, or rupture of the transected aorta. Table 6.2-17 presents the primary safety endpoint results from the study of the Zenith Alpha™ Thoracic Endovascular Graft for BTAI.

Table 6.2-17. Results for the primary safety endpoint (30-day mortality)

Endpoint	Measure	Percent Patients (number/total number)
Safety	30-day all-cause mortality	2.0% (1/50)
	30-day aortic-injury-related mortality	0.0% (0/50)

There were no aortic-injury-related deaths within 30 days of the index procedure. The only death (1200054) was adjudicated as unrelated to BTAI repair by the CEC (death due to respiratory failure), resulting in an all-cause mortality rate of 2.0%.

Four deaths were reported beyond 30 days (1 related to BTAI repair; 3 unrelated to BTAI repair). The one death adjudicated as related to BTAI repair occurred on day 116 due to exsanguination from aortoesophageal fistula (1200024). This same patient previously underwent reintervention on day 74 to treat a pseudoaneurysm proximal to the originally placed stent-graft (see Table 6.2-23), which may have resulted from an infectious process.

Adverse Events

Table 6.2-18 reports the frequency of patients with adverse events in each organ system within 0 to 30 days, 31 to 365 days, or 366 to 730 days following BTAI repair.

Table 6.2-18. Number of patients experiencing adverse events by category

Category	0-30 Days	31-365 Days	366-730 Days
Access site/incision[a]	4	0	0
Cardiovascular[b]	7	1	0
Cerebrovascular/neurological[c]	2	0	0
Gastrointestinal[d]	5	1	0
Pulmonary[e]	20	2	1
Renal/urologic[f]	5	4	0
Vascular[g]	7	5	0
Miscellaneous[h]	22	19	2

Note: The same patient may have experienced events in multiple categories.
[a]Access site/incision events included: hematoma (n=2), infection (n=0), dehiscence (n=0), seroma (n=0), pseudoaneurysm (n=1), hernia (n=0), and wound complication requiring return to the operating room (n=1).
[b]Cardiovascular events included: cardiac arrhythmia requiring intervention (n=7), cardiac arrest (n=1), congestive heart failure (n=0), myocardial infarction (n=0), and refractory hypertension (n=0).
[c]Cerebrovascular/neurological events included: paraplegia (n=0), paraparesis > 30 days (n=0), spinal cord shock (n=0), transient ischemic attack (n=0), and stroke (n=2).
[d]Gastrointestinal events included: bowel obstruction (n=2), infection (n=1), paralytic ileus > 4 days (n=1), mesenteric ischemia (n=0), and bleeding (n=2).
[e]Pulmonary events included: respiratory distress syndrome (n=3), COPD (n=0), pneumonia (n=16), hemothorax (n=2), pneumothorax (n=2), pulmonary edema (n=1), pleural effusion requiring intervention (n=3), and pulmonary embolism (n=2).
[f]Renal/urologic events included: renal failure (n=1), UTI requiring antibiotics (n=7), and serum creatinine rise > 30% above baseline resulting in a persistent value > 2 mg/dl (n=1).
[g]Vascular events included: aortic aneurysm (n=0), aortoesophageal fistula (n=1), aortobronchial fistula (n=0), aortoenteric fistula (n=0), hematoma (n=1), arterial thrombosis (n=1), pseudoaneurysm requiring intervention (n=2), coagulopathy (n=0), deep vein thrombosis (n=6), aortic dissection (n=1), aortic rupture (n=0), and distal embolization with tissue loss (n=0).
[h]Miscellaneous events included: device infection (n=0), hypersensitivity/allergic reaction (n=0), multi-organ failure (n=3), sepsis (n=2), and other (n=30).

There were no ruptures or conversions to open repair within 30 days.

Effectiveness Results

The analysis of effectiveness was based on the 50 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of BTAI. The primary effectiveness endpoint was device success at 30 days. Device success at 30 days was defined as successful access of the injury site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location with patency at the time of deployment completion (technical success), plus none of the following at 30 days: device collapse, Type I or Type III endoleak requiring reintervention, or conversion to open surgical repair. Table 6.2-19 presents the primary effectiveness endpoint results from the study of the Zenith Alpha™ Thoracic Endovascular Graft for BTAI.

Table 6.2-19. Results for the primary effectiveness endpoint (30-day device success)

Endpoint	Measure	Percent Patients (number/total number)
Effectiveness	30-day device success	96.0% (48/50)

Device success was achieved in 96.0% of patients. There were 2 patients (1200012, 1200033) who did not meet the effectiveness endpoint of 30-day device success for the following reasons: 1 patient (1200012) had device compression and 1 patient (1200033) had a site-reported Type I endoleak requiring secondary intervention – note that the compression observed in patient 1200012 was not consistent with collapse of the proximal end of the device (refer to Table 6.2-22 for additional details); nonetheless, the patient was counted as a failure for conservatism.

Beyond 30 days, there was one patient (1200006) who required placement of an additional stent-graft (described in Table 6.2-23) to treat an area of residual injury or possible endoleak (counted as a Miscellaneous/Other event between 31-365 days in Table 6.2-18).

Device Performance

The extent of injury healing, as determined by maximum transverse diameter at the site of injury, observed from the pre-procedure measurement to the 30-day, 6-month, and 12-month follow-up exams (based on core laboratory evaluation), is presented in Table 6.2-20. There were two patients (both at 6 months) who had an increase in diameter > 5 mm at the site of injury when compared to the pre-procedure measurement, which was associated with endoleak in one patient that required secondary intervention followed by conversion to open surgical repair in the setting of graft undersizing. There were no reports of endoleak or secondary intervention in the other patient, nor was there any change in size (< 5 mm change) when compared to the measurement at first follow-up.

Table 6.2-20. Aortic injury size and status based on results from core laboratory analysis

Follow-up*	Result
30-day	
Injury no longer visible (%, n/N)	76.7% (33/43)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)*	1.0 ± 2.3 (n=8, -2.4 – 4.6)
6-month	
Injury no longer visible (%, n/N)	88.2% (30/34)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)*	3.1 ± 3.4 (n=4, -0.3 – 6.3)[a,b]
12-month	
Injury no longer visible (%, n/N)	96.0% (24/25)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)	-0.1 (n=1, -0.1)

*Max diameter change at the site of injury as compared to the pre-procedure measurement applied only if the injury was still visible at follow-up.

[a]Patient 1200058 – The max diameter increased > 5 mm at the site of injury when compared to the pre-procedure measurement; there was no change (≤ 5 mm change) when compared to the measurement at first follow-up. There were no reports of endoleak by the core lab and the patient has not undergone a secondary intervention.

[b]Patient 1200033 – The max diameter increased > 5 mm at the site of injury when compared to the pre-procedure measurement; the patient was reported to have an unknown endoleak type by the core laboratory (proximal Type I endoleak by the site), which required secondary intervention followed by conversion to open surgical repair in the setting of graft undersizing.

Endoleaks classified by type, as assessed by the core laboratory at each exam period, are reported in Table 6.2-21.

Table 6.2-21. Endoleak based on results from core laboratory analysis

Type	Percent Patients(number/total number)		
	30-day[a]	6-month	12-month
Any (new only)	7.1% (3/42)	0	0
Any (new and persistent)	7.1% (3/42)	2.9% (1/34)	0
Multiple	0	0	0
Proximal Type I	0	0	0
Distal Type I	0	0	0

Type	Percent Patients(number/total number)		
	30-day[a]	6-month	12-month
Type II	2.4% (1/42)[b]	0	0
Type III	0	0	0
Type IV	0	0	0
Unknown	4.8% (2/42)[c,d]	2.9% (1/34)[d]	0

[a]Endoleak was not assessed for 1 patient (1200012) due to a suboptimal exam submission (noncontrast exam).
[b]Patient 1200061
[c]Patient 1200035
[d]Patient 1200033 – Patient underwent secondary intervention as described further in Table 6.2-23.

No loss of patency was observed out to 12 months, as assessed by the core laboratory at 30 days. While not a loss in graft patency, one patient (1200060) required placement of an additional stent-graft at 435 days post-procedure (described in Table 6.2-23) to treat thrombus in the distal stent-graft and native aorta (counted as a Miscellaneous/Other event between 366-730 days in Table 6.2-18).

Table 6.2-22 reports device integrity findings based on the results from core laboratory analysis of follow-up imaging.

Table 6.2-22. Device integrity based on results from core laboratory analysis

Finding	Percent Patients (number/total number)		
	30-day	6-month	12-month
Kink	0	0	0
Device compression	2.3% (1/43)[a]	0	0
Device infolding	0	0	0
Stent fracture	0	0	0

[a] Patient 1200012 – Symmetrical compression occurred to the proximal section of the second component that was placed in this patient, due possibly to the component having been deployed through the distal suture loop of the proximal (first) component, which then restricted the second component from fully opening. This finding of compression is considered different from the compression/infolding due to hemodynamic forces commonly associated with the most proximal aspect of a stent-graft. The patient had not experienced any adverse sequelae, but underwent a secondary intervention 335 days post-procedure. Balloon angioplasty was performed and the secondary intervention was deemed successful. Core laboratory analysis of the secondary intervention angiogram revealed no device compression.

Tables 6.2-23 and 6.2-24 summarize the site-reported reasons for secondary intervention and types of secondary intervention, respectively. One patient underwent placement of screws for Type I endoleak. One patient underwent balloon angioplasty for device compression. Four patients underwent secondary interventions involving additional

stent-graft placement (one to treat dissection, one to treat a pseudoaneurysm, one to treat an area of residual injury or possible endoleak, and one to treat an area of thrombus).

Table 6.2-23. Site-reported reasons for secondary intervention

Reason	0-30 Days	31-365 Days	366-730 Days
Device compression	0	1[b]	0
Endoleak			
Type I proximal	1[a]	0	0
Type I distal	0	0	0
Type II	0	0	0
Type III (graft component overlap)	0	0	0
Type III (hole/tear in graft)	0	0	0
Type IV (through graft body)	0	0	0
Unknown	0	0	0
Clinical signs/symptoms	0	1[e]	0
Other	0	2[c,d]	1[f]

[a]Patient 1200033 – The patient was treated for a proximal Type I endoleak (per site assessment; core laboratory reported an unknown type of endoleak) 30 days post-procedure; the graft appeared undersized based on core laboratory-assessed aortic diameter measurements. Six Heli-FX™ screws were placed but the endoleak persisted and the secondary intervention was deemed unsuccessful. The patient later underwent conversion to open surgical repair 181 days after the index procedure. The patient survived the surgery and has not experienced any adverse events subsequent to the conversion as of 212 days post-procedure.

[b]Patient 1200012 underwent balloon angioplasty 335 days post-procedure to correct device compression of the proximal section of the second component (with no associated adverse sequelae) noted on the 1-month CT scan (refer to additional details in Table 6.2-22). The secondary intervention was deemed successful.

[c]Patient 1200024 underwent two secondary interventions following the index procedure. An unsuccessful secondary intervention (stent-graft placement) was attempted to treat a pseudoaneurysm proximal to the previously placed stent-graft (counted as a Vascular event in Table 6.2-18) on post-procedure day 74. On post-procedure day 79, the patient underwent a mini-sternotomy, aortic arch debranching, aortic bypass to the innominate and left carotid arteries with Hemashield™ graft, placement of a commercially available endograft, and bilateral chest tube placement to successfully treat the pseudoaneurysm. As described previously, the patient subsequently died on post-operative day 116. The death was adjudicated as procedure-related by the CEC (cause of death was exsanguination due to aortoesophageal fistula).

[d]Patient 1200006 underwent placement of a commercially available stent-graft 219 days post-procedure to treat an area of residual injury or possible endoleak (counted as a Miscellaneous/Other event in Table 6.2-18). The injury was incompletely treated during the index procedure due to the device having been placed too far distally (noted on the 6- month CT scan). The patient also required a left subclavian artery bypass. The secondary intervention was deemed successful.

[e]Patient 1200036 was diagnosed with an aortic dissection distal to the previously placed stent-graft (counted as a Vascular event in Table6.2-18) on post-operative day 286 after returning to the hospital for chest pain. The site noted that the patient was hypertensive and had stopped taking his blood pressure medication. An additional stent graft was placed the following day, which resolved the patient's symptoms. The patient was discharged 2 days after the reintervention.

[f]Patient 1200060 required placement of an additional stent-graft (overlapped with the existing graft) 435 days post-procedure to treat thrombus in the distal stent-graft and native aorta that was noted on the 12-month CT scan (counted as a Miscellaneous/Other event in Table 6.2-18). The site reported that the intervention was successful.

Table 6.2-24. Types of secondary interventions

Type*	0-30 Days	31-365 Days	366 – 730 Days
Percutaneous			
Additional proximal component	0	1[d]	1[f]
Balloon angioplasty	0	1[b]	0
Stent	0	2[c,e]	0
Other	0	0	0
Surgical			
Conversion to open repair	0	0	0
Other	1[a]	2[c,d]	0
Other	0	0	0

*A patient may have had more than one treatment type.
[a-f]Refer to footnotes in Table 6.2-23 for additional details.

Longer-term Follow-up

The information obtained > 30 days following endovascular repair appears consistent with results through 30 days with respect to morbidity, mortality, and device performance. The only event types observed during longer-term follow-up that were not previously observed within 30 days were aortic-injury-related death in one patient who developed an aortoesophageal fistula, aortic dissection distal to the endovascular graft in one patient who had stopped taking their blood pressure medications and was treated with placement of an additional endovascular graft component, and one patient who underwent conversion to open surgical repair due to the site-reported reason of proximal Type I endoleak in the setting of an undersized graft.

Summary

This study enrolled 50 patients treated with the Zenith Alpha™ Thoracic Endovascular Graft for BTAI. All but one patient received a single study component at the index procedure (one patient received two study components). One patient who received a single study component also received two commercially available components; the first study component and first commercial component placed were the same diameter and had been undersized as measurements were from a pre-procedure CT scan performed while the patient was not fully resuscitated, prompting additional labelling instruction that graft sizing for BTAI should be based on measurements in a fully resuscitated patient. All grafts were deployed successfully in the intended location, and all graft components were patent upon completion of deployment, yielding a technical success rate of 100%.

There was one death within 30 days of endovascular repair, which was adjudicated by an independent CEC as not related to the BTAI repair. There were no ruptures reported at any follow-up time point. There were no conversions to open repair within the first 30 days following the index procedure. Patients experienced adverse events in each of the organ system categories.

There were no core laboratory-identified Type I or Type III endoleaks, device migrations, device infolding, or stent fractures. One occurrence of device compression was noted without any adverse clinical sequelae, and resolved after a secondary intervention. One patient underwent successful conversion to open surgical repair 181 days post-procedure (due to a site-reported Type I endoleak that was the result of graft undersizing) and remained alive beyond 30 days following the conversion procedure. There was one aortic-injury-related death, which occurred greater than 30 days after the index procedure (in a patient with aortoesophageal fistula).

The results for the primary safety and effectiveness endpoints were within the expected ranges for treatment of patients with BTAI. Overall, the results provide a reasonable assurance of safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of BTAI.

6.3. Summary of Supplemental Clinical Information

6.3.1. Longer-term Follow-up (> 2 years) – Aneurysm/Ulcer Pivotal Study

As of April 7, 2015 there were 34 patients eligible for follow-up beyond 2 years (as shown in Table 6.1-2). Three patient deaths have been reported > 730 days following endovascular repair (2 of which were CEC-adjudicated as not related to TAA-repair and 1 which the CEC was unable to adjudicate). There are no reports of rupture or conversion to open surgical repair > 730 days. One additional patient experienced aneurysm growth (> 5 mm) after 2 years, which was associated with an inadequate landing zone length. There were no new reports of migration or Type I or III endoleak beyond 2 years. One new stent fracture was identified at 3 years, without adverse clinical sequelae. Three patients have undergone reintervention beyond 2 years, each of which was described previously due to having exhibited aneurysm growth within 2 years (one patient also had distal Type I endoleak and migration within 2 years, while another also had distal Type I endoleak within 2 years).

6.3.2. Continued Access – Aneurysm/Ulcer Indication

The results from patients treated during the continued access investigation of the aneurysm/ulcer indication (n = 18) were consistent with the results described for the pivotal study cohort, including one patient with aneurysm growth and Type I endoleak (at 6 months) that was associated with graft undersizing following initial treatment of the aneurysm with only a proximal component. Additionally, a portion of the patients enrolled in the continued access investigation (n = 11) were treated with the rotation handle version of the introduction system, which successfully deployed the stent-graft in all cases, consistent with the deployment results based on bench testing.

6.3.3. European Post-market Survey – Delivery System with Rotational Handle

A post-market survey was implemented in Europe to gather additional supportive information regarding clinical performance of the rotation handle introduction system. Physician users in Europe were surveyed on the procedural performance of the rotation handle system beginning March 31, 2014. A total of 38 surveys were completed as of June 30, 2014. Table 6.3.3-1 summarizes the survey results.

Table 6.3.3-1. Results of European post-market survey

Survey Question	Response Percent (number/total number)	
Did the introduction system with the rotation handle successfully retract the release-wires without the use of the alternate sequence?	Yes	100% (38/38)
	No	0
Was the alternate sequence successful in retracting the release-wires?	Yes	Not applicable
	No	Not applicable
	Not applicable	100% (38/38)
Was the graft successfully deployed in the intended location?	Yes	97.4% (37/38)
	No	2.6% (1/38)[a]
Was the graft patent at the completion of the procedure?	Yes	100% (38/38)
	No	0

[a]Slight distal migration of a tapered proximal component was reported.

All grafts were successfully deployed in the intended location using the primary release sequence, as described in the IFU, with the exception of one report of a slight distal migration during deployment. The alternate release sequence, which is also described in the IFU and is intended to be used in situations in which deployment difficulties involving the handle are encountered, was not used in any case. Furthermore, all grafts were patent at the completion of the procedure and no unique findings were observed as compared to the results from the pivotal clinical studies. These results in combination

with the results from the preclinical studies and uses of the introduction system with rotation handle during continued access provide a reasonable assurance of safety and effectiveness of the modifications that were made to the user interface since the time of enrollment completion in the pivotal clinical studies.

TMM: Note that the font will be edited for the final print

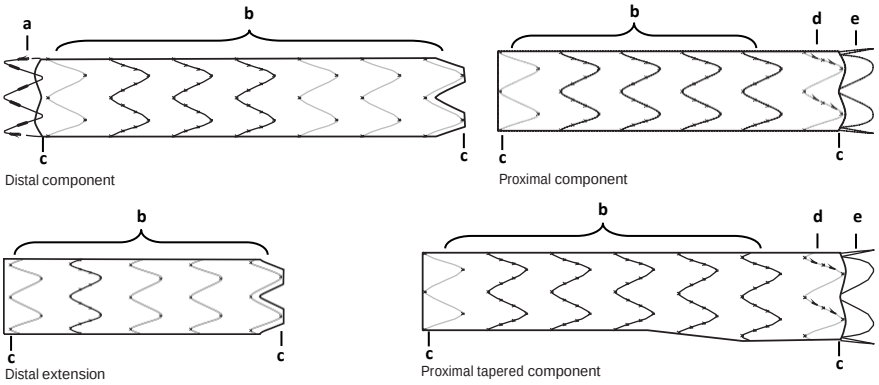
Clinical Summary is a separate document and will be made available online.

Zenith Alpha™ Thoracic Endovascular Graft

Instructions for Use

Patient I.D. Card Included

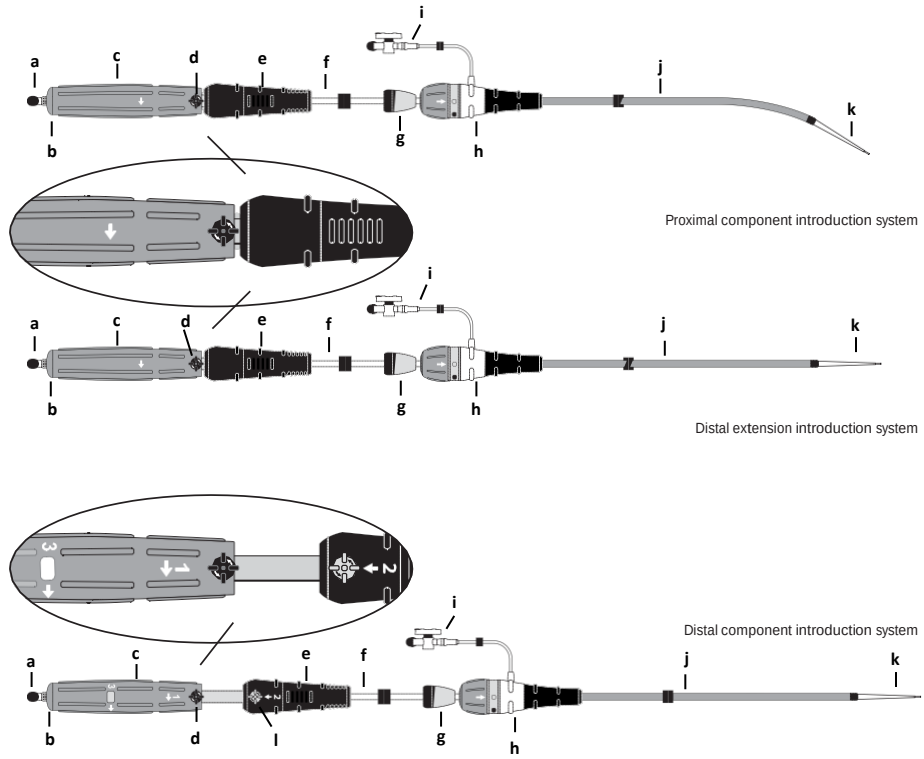
TABLE OF CONTENTS



1

Stent Graft Components

a. Distal bare stent with barbs
b. Body stent (internal or external)
c. Gold radiopaque markers (located near stent apices on proximal and distal edges of graft)
d. Proximal sealing stent with barbs
e. Bare alignment stent

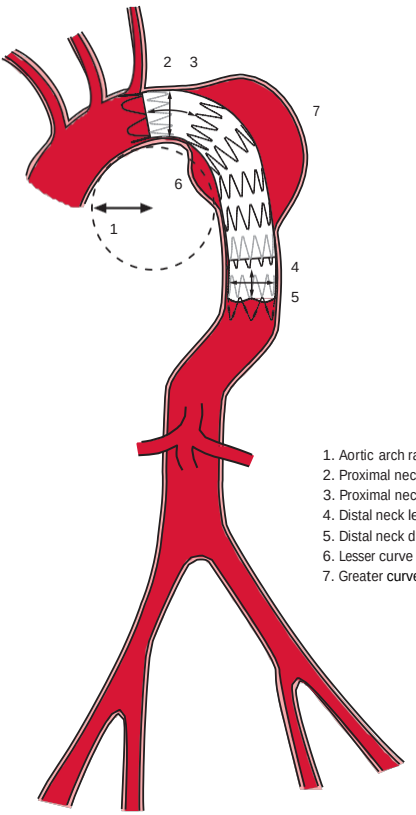


l_2

Introduction System Components

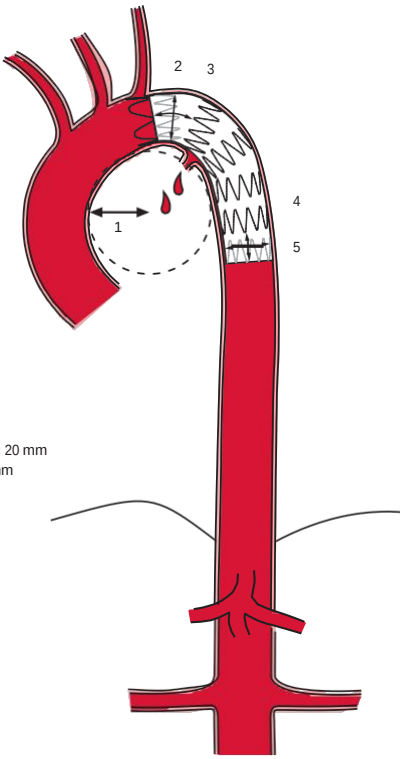
a. Cannula hub
b. Back-end cap
c. Blue rotation handle
d. Black safety-lock knob
e. Black gripper (telescoping on distal component)
f. Gray positioner
g. Captor sleeve
h. Captor hemostatic valve
i. Connecting tube with stopcock
j. Flexor sheath
k. Dilator tip
l. Gray safety-lock knob

3

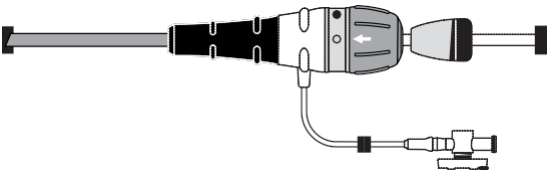


1. Aortic arch radius of curvature ≥ 20 mm
2. Proximal neck diameter 15-42 mm
3. Proximal neck length ≥ 20 mm
4. Distal neck length ≥ 20 mm
5. Distal neck diameter 15-42 mm
6. Lesser curve
7. Greater curve

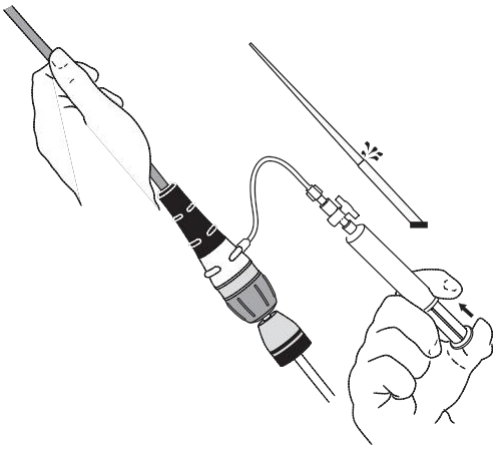
3



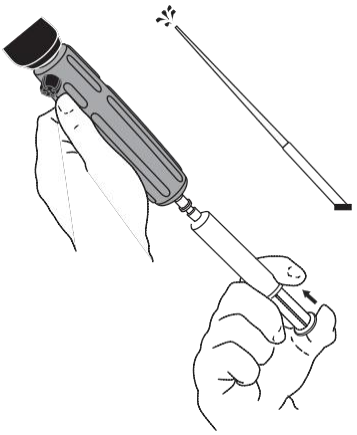
4



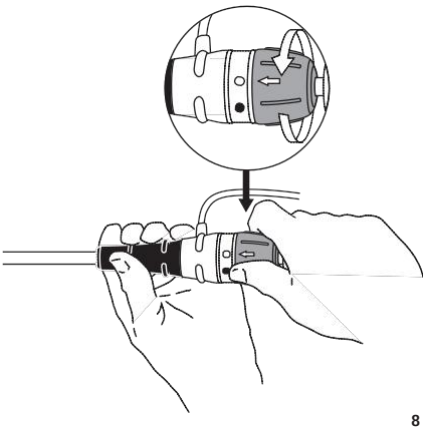
5



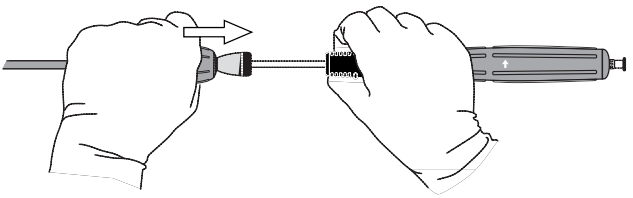
6



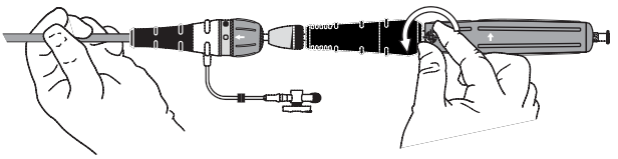
7



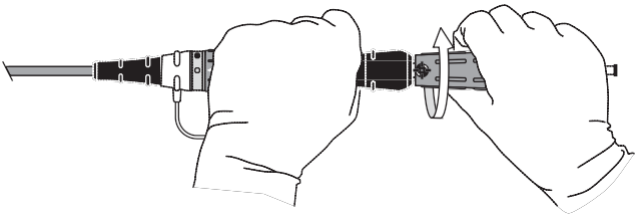
8



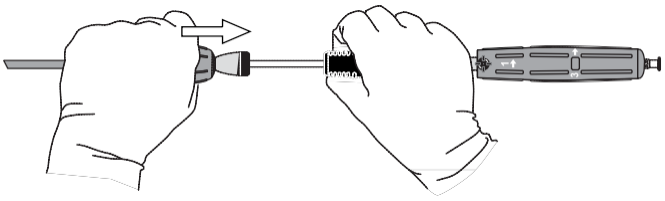
9



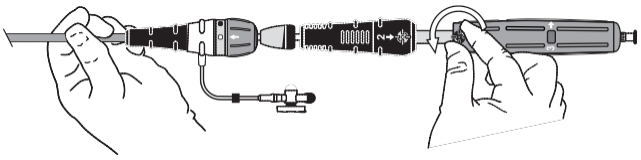
10



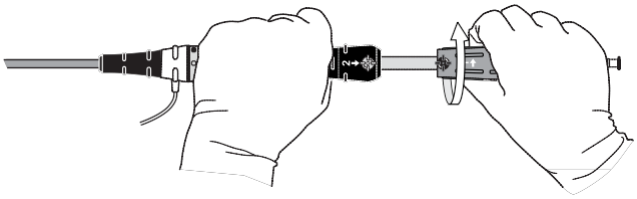
11



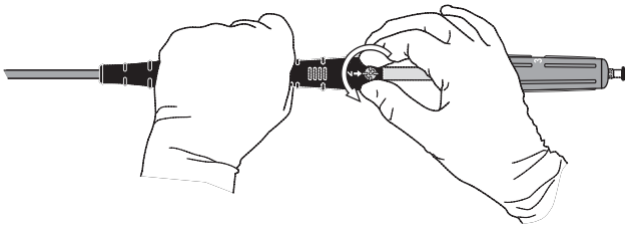
12



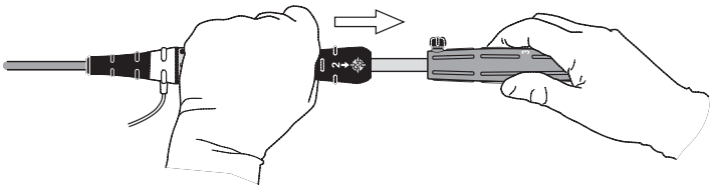
13



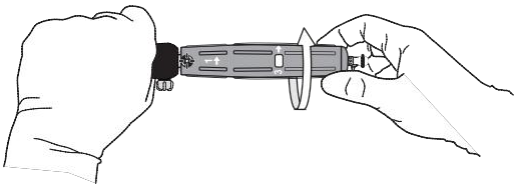
14



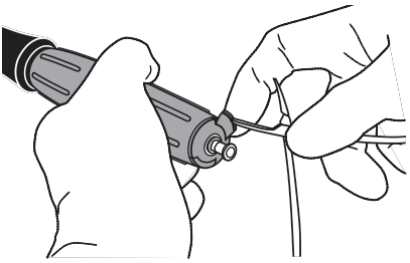
15



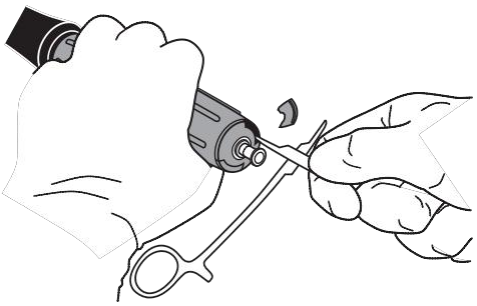
16



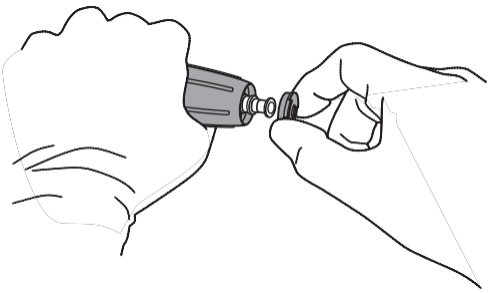
17



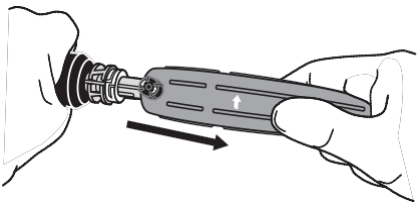
18



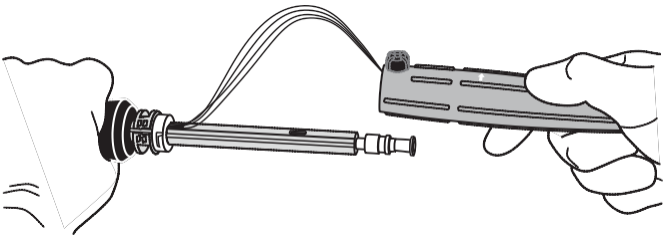
19



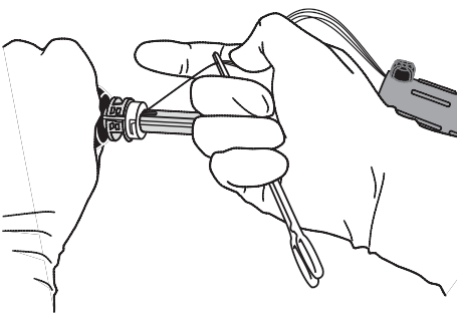
20



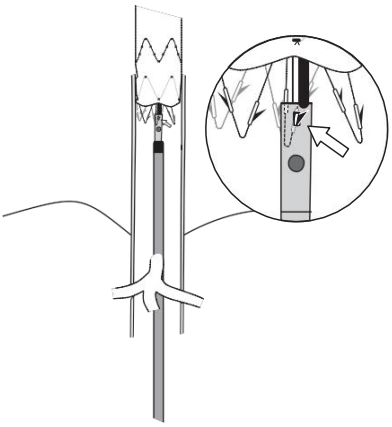
21



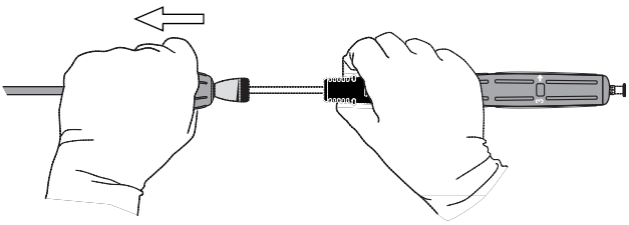
22



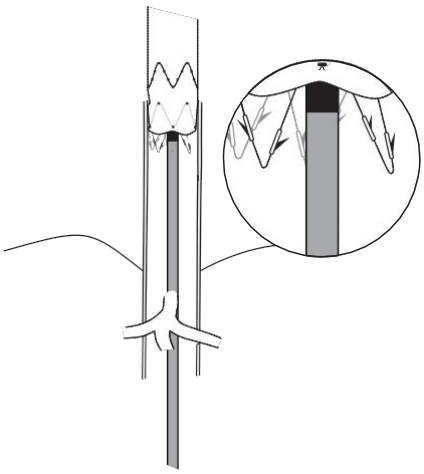
23



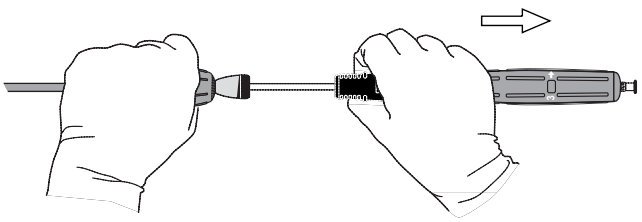
24



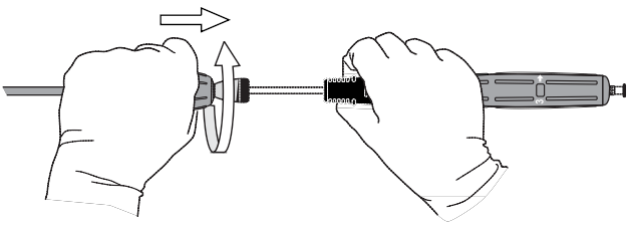
25



26



27



28

ZENITH ALPHA™ THORACIC ENDOVASCULAR GRAFT

Read all instructions carefully. Failure to properly follow the instructions, warnings, and precautions may lead to serious consequences or injury to the patient.

CAUTION: U.S. federal law restricts this device to sale by or on the order of a physician (or a properly licensed practitioner).

CAUTION: All contents of the inner pouch (including the introduction system and endovascular graft) are supplied sterile, for single use only.

1 DEVICE DESCRIPTION

1.1 Zenith Alpha Thoracic Endovascular Graft

The Zenith Alpha Thoracic Endovascular Graft is a two-piece cylindrical endovascular graft consisting of proximal and distal components. The proximal component can be either tapered or nontapered and may be used independently (for ulcers/saccular aneurysms or blunt thoracic aortic injuries) or in combination with a distal component. The stent grafts are constructed of woven polyester fabric sewn to self-expanding nitinol stents with braided polyester and monofilament polypropylene suture. **(Fig. 1)** Both components are fully stented to provide stability and the expansile force necessary to open the lumen of the graft during deployment. Additionally, the nitinol stents provide the necessary attachment and seal of the graft to the vessel wall.

To assist with alignment, the proximal component has an uncovered stent. For added fixation and sealing, the proximal component has an internal sealing stent with fixation barbs that protrude through the graft material. In addition, the bare stent at the distal end of the distal component also contains barbs. On devices with diameters of 40-46 mm, the proximal sealing stent remains constrained to ensure alignment with the inner curvature of the aorta.

To facilitate fluoroscopic visualization of the stent graft, gold radiopaque markers are positioned on each end of the proximal and distal components. Gold markers are placed on stent apices at the proximal and distal aspects of the graft margins, denoting the edge of the graft material, to assist with deployment accuracy.

1.2 Introduction System

The Zenith Alpha Thoracic Endovascular Graft is shipped preloaded onto an introduction system. It has a sequential deployment method with built-in features to provide continuous control of the endovascular graft throughout the deployment procedure. The introduction system enables precise positioning before deployment of the proximal and distal components.

The main body graft components are deployed from a 16 French (6 mm OD), 18 French (7.1 mm OD), or 20 French (7.7 mm OD) introduction system. The proximal component's introduction system is slightly precurved to assist in proximal inferior wall apposition of the graft during deployment. (**Fig. 2**) These systems use either a single locking mechanism (for the proximal component and distal extension) or dual locking mechanisms (for the distal component) to secure the endovascular graft onto the introduction system until the physician releases it. All introduction systems are compatible with a .035 inch wire guide.

The introduction system features a Flexor® introducer sheath with a Captor Hemostatic Valve. For added hemostasis, the Captor Hemostatic Valve can be loosened or tightened for the introduction and/or removal of ancillary devices into and out of the sheath. The Flexor introducer sheath resists kinking and is hydrophilically coated. Both features are intended to enhance trackability in the iliac arteries and thoracic aorta.

1.3 Zenith Alpha Thoracic Endovascular Graft Ancillary Component

An endovascular ancillary component is available. The Zenith Alpha Thoracic Endovascular Graft ancillary component is a cylindrical component constructed from the same woven polyester fabric, self-expanding nitinol stents, and polyester and polypropylene suture used in the main body graft components. At the distal and proximal graft margins, the z-stents are attached to the inner surface for enhanced sealing. (**Fig. 1**) The ancillary component can be used to provide additional length to the endovascular graft distally or to increase the length of overlap between components. Additionally, the proximal component may be used to extend graft coverage proximally.

The Zenith Alpha Thoracic Endovascular Graft Distal Extension is deployed from a 16 French (6 mm OD), 18 French (7.1 mm OD), or 20 French (7.7 mm OD) introduction system. (**Fig. 2**) A single locking mechanism secures the endovascular graft to the introduction system until it is released by the physician. The locking mechanism is released by turning the rotation handle. All systems are compatible with a .035 inch wire guide.

To facilitate fluoroscopic visualization of the distal extension, gold radiopaque markers are positioned on the ends of the graft. Gold markers are placed on stent apices at the proximal and distal aspects of the graft margins, denoting the edge of the graft material, to assist with deployment accuracy.

2 INDICATIONS FOR USE

The Zenith Alpha Thoracic Endovascular Graft is indicated for the endovascular treatment of patients with isolated lesions of the descending thoracic aorta (not including dissections) having vascular anatomy suitable for endovascular repair, (**Fig. 3** and **Fig. 4**), including:

- Iliac/femoral anatomy that is suitable for access with the required introduction systems,
- Nonaneurysmal aortic segments (fixation sites) proximal and distal to the thoracic lesion:
  - with a length of at least 20 mm, and
  - with a diameter measured outer-wall-to-outer-wall of no greater than 42 mm and no less than 15 mm.

3 CONTRAINDICATIONS

The Zenith Alpha Thoracic Endovascular Graft is contraindicated in:

- Patients with known sensitivities or allergies to polyester, polypropylene, nitinol, or gold.
- Patients who have a condition that threatens to infect the endovascular graft.

4 WARNINGS AND PRECAUTIONS

4.1 General

- Read all instructions carefully. Failure to properly follow the instructions, warnings, and precautions may lead to serious consequences or injury to the patient.
- The Zenith Alpha Thoracic Endovascular Graft should be used only by physicians and teams trained in vascular interventional techniques (catheter based and surgical) and in the use of this device. Specific training expectations are described in **Section 10.1, Physician Training.**
- Additional endovascular interventions or conversion to standard open surgical repair following initial endovascular repair should be considered for patients experiencing enlarging aneurysms or ulcers, unacceptable decrease in fixation length (vessel and component overlap) and/or endoleak. An increase in aneurysm or ulcer size and/or persistent endoleak or migration may lead to rupture of the aneurysm or ulcer.
- Patients experiencing leaks or reduced blood flow through the graft may be required to undergo secondary endovascular interventions or surgical procedures.
- Always have a qualified surgery team available during implantation or reintervention procedures in the event that conversion to open surgical repair is necessary.

4.2 Patient Selection, Treatment and Follow-Up

- The Zenith Alpha Thoracic Endovascular Graft is designed to treat aortic neck diameters no smaller than 15 mm and no larger than 42 mm. The Zenith Alpha Thoracic Endovascular Graft is designed to treat proximal aortic necks (distal to either the left subclavian or left common carotid artery) of at least 20 mm in length. Additional proximal aortic neck length may be gained by covering the left subclavian artery (with or without discretionary transposition) when necessary to optimize device fixation and maximize aortic neck length. Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends. A distal aortic neck length of at least 20 mm proximal to the celiac axis is required. These sizing measurements are critical to the performance of the endovascular repair. In patients with large proximal aortic vessel diameter and aneurysms on the inner curvature, there is a risk that the graft may deploy in an angulated position if the sealing zone is less than 20 mm.
- Adequate iliac or femoral access is required to introduce the device into the vasculature. Careful evaluation of vessel size, anatomy, and disease state is required to ensure successful sheath introduction and subsequent withdrawal, as vessels that are significantly calcified, occlusive, tortuous, or thrombus lined may preclude introduction of the endovascular graft and/or increase the risk of embolization. A vascular conduit technique may be necessary to achieve access in some patients.
- Key anatomic elements that may affect successful exclusion of the thoracic lesion include severe angulation (radius of curvature < 20 mm and localized angulation > 45 degrees); short proximal or distal fixation sites (< 20 mm); an inverted funnel shape at the proximal fixation site or a funnel shape at the distal fixation site (greater than a 10% change in diameter over 20 mm of fixation site length); and circumferential thrombus and/or calcification at the arterial fixation sites. Irregular calcification and/or plaque may compromise the attachment and sealing at the fixation sites. In the presence of anatomical limitations, a longer neck length may be required to obtain adequate sealing and fixation. Necks exhibiting these key anatomic elements may be more conducive to graft migration. In patients with large aneurysms on the outer curvature close to the left subclavian, it may be difficult to track the device around the arch, and extra support may be needed using a brachio-femoral wire. If difficulty is noted in tracking the second component through tortuous anatomy of the thoracic aorta, extra support may be provided using a brachio-femoral wire.
- The safety and effectiveness of the Zenith Alpha Thoracic Endovascular Graft and ancillary components have not been evaluated in the following patient populations:
  - aortobronchial and aortoesophageal fistulas
  - aortitis or inflammatory aneurysms
  - diagnosed or suspected genetic connective tissue disease (e.g., Marfans or Ehlers-Danlos Syndrome)
  - dissections
  - females who are pregnant, breastfeeding, or planning to become pregnant within 60 months
  - leaking, pending rupture or ruptured aneurysm
  - patients less than 18 years of age
  - mycotic aneurysms
  - pseudoaneurysms resulting from previous graft placement
  - systemic infection (e.g., sepsis)
  - access vessels that preclude safe insertion
  - inability to preserve the left common carotid artery and celiac artery
  - previous repair in descending thoracic aorta
  - surgical or endovascular AAA repair within 30 days before or after TAA repair
  - bleeding diathesis, uncorrectable coagulopathy, or refuses blood transfusion
  - stroke within 3 months
  - untreatable reaction to contrast, which cannot be adequately premedicated
- Successful patient selection requires specific imaging and accurate measurements; please see **Section 4.3, Pre-Procedure Measurement Techniques and Imaging.**
- If occlusion of the left subclavian artery ostium is required to obtain adequate neck length for fixation and sealing, transposition or bypass of the left subclavian artery may be warranted.
- The Zenith Alpha Thoracic Endovascular Graft is not recommended for patients who cannot tolerate contrast agents necessary for intraoperative and postoperative follow-up imaging, or who are unable to undergo, or will not be compliant with the necessary preoperative and postoperative imaging and implantation studies as described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP**. All patients should be monitored closely and checked periodically for change in the condition of their disease and the integrity of the endoprosthesis.
- The Zenith Alpha Thoracic Endovascular Graft is not recommended for patients whose weight and/or size would compromise or prevent the necessary imaging requirements.
- Graft implantation may increase the risk of paraplegia or paraparesis where graft exclusion covers the origins of dominant spinal cord or intercostal arteries.
  - **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the endovascular graft) should receive enhanced follow-up. Specific follow-up guidelines are described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP.**
  - The long-term performance of endovascular grafts has not yet been established in young patients and patients performing extreme sports.
  - After endovascular graft placement, patients should be regularly monitored for endoleak flow, thoracic lesion growth, or changes in the structure or position of the endovascular graft.

4.3 Pre-Procedure Measurement Techniques and Imaging

- All lengths and diameters of the devices necessary to complete the procedure should be available to the physician, especially when pre-operative case planning measurements (treatment diameters/lengths) are not certain. This approach allows for greater intra-operative flexibility to achieve optimal procedural outcomes.
- Lack of non-contrast CT imaging may result in failure to appreciate iliac or aortic calcification that may preclude access or reliable device fixation and seal.
- Pre-procedure imaging reconstruction thicknesses > 3 mm may result in suboptimal device sizing, or in failure to appreciate focal stenoses from CT.
- Clinical experience indicates that contrast-enhanced spiral computed tomographic angiography (CTA) with 3-D reconstruction is the strongly recommended imaging modality to accurately assess patient anatomy prior to treatment with the Zenith Alpha Thoracic Endovascular Graft. If contrast-enhanced spiral CTA with 3-D reconstruction is not available, the patient should be referred to a facility with these capabilities.
- Clinicians recommend positioning the x-ray C-arm during procedural angiography so that it is perpendicular to the aortic vessel neck proximal to the thoracic lesion, typically 45-75 degrees left anterior oblique (LAO) for the arch.

- **Diameter:** A contrast-enhanced spiral CTA is strongly recommended for measuring aortic diameter. Diameter measurements should be determined from the outer-wall-to-outer-wall vessel diameter and not the lumen diameter. The spiral CTA scan must include the great vessels through the femoral heads at an axial slice thickness of 3 mm or less. **For blunt thoracic aortic injury patients, CTA measurements should be based on a CTA of a fully resuscitated patient**.
- Clinical experience has shown that temporary changes in aortic diameter during blood loss can lead to incorrect aortic measurement on preoperative CTA, inadequate sizing, and increased risks of graft complications, migration and endoleak, as observed during the clinical study. If preoperative CTA is done during hemodynamic instability, repeat CTA when the patient is stable or use IVUS at the time of the procedure to confirm diameter measurements. For patients with blunt thoracic aortic injuries, if there is significant periaortic hematoma in the region of the subclavian artery the hematoma should not be counted in the diameter measurement, as there is a risk of oversizing the graft.
- **Length:** Clinical experience indicates that 3-D CTA reconstruction is the strongly recommended imaging modality to accurately assess proximal and distal neck lengths for the Zenith Alpha Thoracic Endovascular Graft. These reconstructions should be performed in sagittal, coronal, and varying oblique views depending upon individual patient anatomy. If 3-D reconstruction is not available, the patient should be referred to a facility with these capabilities. **Length measurements should be taken along the greater curvature of the aorta, including the aneurysm, if present.**

  NOTE: The greater curvature is the longest measurement following the curve of the aneurysm and may be on the outer or inner curvature of the aorta depending on the location of the aneurysm.

  NOTE: Large aneurysms and difficult anatomy may require extra care in planning.

4.4 Device Selection

- **Strict adherence to the Zenith Alpha Thoracic Endovascular Graft IFU sizing guide both in terms of component diameter (Tables 1 and 2 in Section 10.5 Device Diameter Sizing Guidelines) as well as component type/length (as stated below and in Section 10.6 Device Length Sizing Guidelines) is strongly recommended in order to mitigate the risk for events (e.g., migration, endoleak, aneurysm growth) that could result from selecting inappropriate device sizes**.
- **Tables 1** and **2** incorporate appropriate device oversizing. Sizing outside of the recommendations provided in Tables 1 and 2, including that which could result from a difference in location of graft deployment relative to the location used for graft sizing, can result in aneurysm growth, endoleak, and migration, as observed in the clinical studies (refer to the Device Performance sections in the SUMMARY OF CLINICAL DATA). Fracture, device infolding, or compression may also result.
- Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends.
- To treat more focal aortic injuries, as often found in blunt thoracic aortic injury patients, a proximal component can be used alone.
- In aneurysms the graft may settle into the greater curve of the aneurysm over time. Accordingly, extra graft length needs to be planned.
  - A two-component repair (proximal and distal component) is recommended, as it provides the ability to adapt to the length change over time. A two-component repair (proximal and distal component) also provides active fixation at both the proximal and distal seal sites.
  - The minimum required amount of overlap between devices is three stents. Less than a three-stent overlap may result in endoleak (with or without component separation). However, no part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall. Device lengths should be selected accordingly.
  - If an acceptable two-component (proximal and distal component) treatment plan cannot be achieved (e.g., excessive aortic coverage, even with maximal overlap of shortest components), the proximal component must be selected with enough length to achieve and maintain the minimum 20 mm sealing zones at both ends even when positioned in the greater curve of the aneurysm. Failure to do so could result in migration, endoleak, and aneurysm growth, as observed in the clinical study (refer to the Device Performance section in the SUMMARY OF CLINICAL DATA from the aneurysm/ulcer study).

4.5 Implant Procedure

- Systemic anticoagulation should be used during the implantation procedure based on hospital- and physician-preferred protocol. If heparin is contraindicated, an alternative anticoagulant should be used.
- Appropriate procedural imaging is required to successfully position the Zenith Alpha Thoracic Endovascular Graft and ensure accurate apposition to the aortic wall.
- Fluoroscopy should be used during introduction and deployment to confirm proper operation of the introduction system components, proper placement of the graft, and desired procedural outcome.
- The use of the Zenith Alpha Thoracic Endovascular Graft requires administration of intravascular contrast. Patients with pre-existing renal insufficiency may have an increased risk of renal failure postoperatively. Care should be taken to limit the amount of contrast media used during the procedure, and to observe preventative methods of treatment to decrease renal compromise (e.g., adequate hydration).
- Use caution during manipulation of catheters, wires, and sheaths within the thoracic lesion. Significant disturbances may dislodge fragments of thrombus or plaque, which can cause distal or cerebral embolization, or cause rupture of the thoracic lesion or aorta.
- Minimize handling of the constrained endoprosthesis during preparation and insertion to decrease the risk of endoprosthesis contamination and infection.
- To activate the hydrophilic coating on the outside of the Flexor introducer sheath, the surface must be wiped with sterile gauze pads soaked in saline solution. Always keep the sheath hydrated for optimal performance.
- Maintain wire guide position during introduction system insertion.
- Do not bend or kink the introduction system. Doing so may cause damage to the introduction system and the Zenith Alpha Thoracic Endovascular Graft.
- To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.
- To avoid damage to the sheath, be careful to advance all components of the system together (from outer sheath to inner cannula).
- Do not continue advancing the wire guide or any portion of the introduction system if resistance is felt. Stop and assess the cause of resistance; vessel, catheter, or graft damage may occur. Exercise particular care in areas of stenosis, intravascular thrombosis, or calcified or tortuous vessels.
- As the sheath and/or wire guide is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check the position as necessary.
- During sheath withdrawal, the uncovered proximal stent and covered proximal stent with barbs are in contact with the vessel wall. At this stage it may be possible to advance the device, but retraction may cause aortic wall damage.
- Inaccurate placement and/or incomplete sealing of the Zenith Alpha Thoracic Endovascular Graft within the vessel may result in increased risk of endoleak, migration, or inadvertent occlusion of the left subclavian, left common carotid, and/or celiac arteries.
- Inadequate fixation of the Zenith Alpha Thoracic Endovascular Graft may result in increased risk of migration of the stent graft. Incorrect deployment or migration of the stent graft may require surgical intervention.
- Inadvertent partial deployment or migration of the endoprosthesis may require surgical removal.
- Land the proximal and the distal ends of the device in parallel aortic neck segments without acute angulation (> 45 degrees) or circumferential thrombus/calcification to ensure fixation and seal.
- Be sure to land the proximal and distal ends of the device in an aortic neck segment with a diameter that matches the initial sizing of the device. Landing in a segment that is < 10% or > 25% of the diameter to which the device was sized may potentially result in inadequate sizing and therefore migration, endoleak, thoracic lesion growth, or increased risk of thrombosis.
- The Zenith Alpha Thoracic Endovascular Graft incorporates an uncovered proximal stent, a covered proximal stent (on the proximal component) with fixation barbs, and an uncovered distal stent (on the distal component) with fixation barbs. Exercise extreme caution when manipulating interventional and angiographic devices in the region of the uncovered proximal stent and uncovered distal stent.
- When using a distal component, take care to avoid landing the distal bare stent in tortuous anatomy (i.e., localized angulation > 45 degrees).
- Unless medically indicated, do not deploy the Zenith Alpha Thoracic Endovascular Graft in a location that will occlude arteries necessary to supply blood flow to organs or extremities. Do not cover significant arch or mesenteric arteries (exception may be the left subclavian artery) with the device. Vessel occlusion may occur. If a left subclavian artery is to be covered with the device, the clinician should be aware of the possibility of compromise to cerebral and upper limb circulation and collateral circulation to the spinal cord.
- Take care not to advance the sheath while the stent graft is still within it. Advancing the sheath at this stage may cause the barbs to perforate the introducer sheath.
- Do not attempt to resheath the graft after partial or complete deployment.
- Repositioning the stent graft distally after partial deployment of the covered proximal stent may result in damage to the stent graft and/or vessel injury.
- To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.
- In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers demonstrate that there is adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.

  NOTE: If endoleaks or other problems are observed, (e.g., inadequate seal length or overlap length) refer to **Section 11.2, Ancillary Devices: Distal Extensions**.
- In the event that reinstrumentation (secondary intervention) of the graft is necessary, avoid damaging the graft or disturbing the graft's position.

4.6 Molding Balloon Use – Optional

- Do not inflate the balloon in the aorta outside of the graft, as doing so may cause damage to the aorta. Use the molding balloon in accordance with its labeling.
- Use care when inflating the balloon within the graft in the presence of calcification, as excessive inflation may cause damage to the aorta.
- Confirm complete deflation of the balloon prior to repositioning.
- For added hemostasis, the Captor Hemostatic Valve can be loosened or tightened to accommodate the insertion and subsequent withdrawal of a molding balloon.

4.7 MRI Safety Information

Nonclinical testing has demonstrated that the Zenith Alpha Thoracic Endovascular Graft is MR Conditional according to ASTM F2503. A patient with this endovascular graft can be scanned safely in a 1.5 T or 3.0 T MR system using the specific testing parameters described in Section 12.4. Additional MRI safety information is found in Section 12.4.

5 POTENTIAL ADVERSE EVENTS

Adverse events associated with either the Zenith Alpha Thoracic Endovascular Graft or the implantation procedure that may occur and/or require intervention include, but are not limited to:

- Amputation
- Anesthetic complications and subsequent attendant problems (e.g., aspiration)
- Aneurysm enlargement
- Aneurysm rupture and death
- Aortic damage, including perforation, dissection, bleeding, rupture and death
- Aortic valve damage
- Aorto-bronchial fistula
- Aorto-esophageal fistula
- Arterial or venous thrombosis and/or pseudoaneurysm
- Arteriovenous fistula
- Bleeding, hematoma, or coagulopathy
- Bowel complications (e.g., ileus, transient ischemia, infarction, necrosis)
- Cardiac complications and subsequent attendant problems (e.g., arrhythmia, tamponade, myocardial infarction, congestive heart failure, hypotension, hypertension)
- Claudication (e.g., buttock, lower limb)
- Death
- Edema
- Embolization (micro and macro) with transient or permanent ischemia or infarction
- Endoleak
- Endovascular graft: improper component placement, incomplete component deployment, component migration and/or separation, suture break, occlusion, infection, stent fracture, stent corrosion, graft material wear, dilatation, erosion, puncture, perigraft flow, barb separation
- Femoral neuropathy
- Fever and localized inflammation
- Genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, fistula, urinary incontinence, hematuria, infection)
- Hepatic failure
- Impotence
- Infection of the aneurysm, device or access site, including abscess formation, transient fever and pain
- Lymphatic complications and subsequent attendant problems (e.g., lymph fistula, lymphocele)
- Local or systemic neurologic complications and subsequent attendant problems (e.g., stroke, transient ischemic attack, paraplegia, paraparesis, spinal cord shock, paralysis)
- Occlusion of coronary arteries
- Pulmonary embolism
- Pulmonary/respiratory complications and subsequent attendant problems (e.g., pneumonia, respiratory failure, prolonged intubation)
- Renal complications and subsequent attendant problems (e.g., artery occlusion, contrast toxicity, insufficiency, failure)
- Surgical conversion to open repair
- Vascular access site complications, including infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula
- Vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death)
- Vessel damage
- Wound complications and subsequent problems (e.g., dehiscence, infection)

DEVICE RELATED ADVERSE EVENT REPORTING

Any adverse event (clinical incident) involving the Zenith Alpha Thoracic Endovascular Graft should be reported to COOK immediately. To report an incident, call the Customer Relations Department at 1-800-457-4500 (24 hour) or 1-812-339-2235.

6 SUMMARY OF CLINICAL DATA

A summary of the clinical data can be found on **www.cookmedical.com.**

7 PATIENT SELECTION AND TREATMENT

(See **Section 4, WARNINGS AND PRECAUTIONS**)

7.1 Individualization of Treatment

Cook recommends that the Zenith Alpha Thoracic Endovascular Graft component diameters be selected as described in **Tables 1** and **2**. All lengths and diameters of the devices necessary to complete the procedure should be available to the physician, especially when preoperative case planning measurements (treatment diameters and lengths) are not certain. This approach allows for greater intraoperative flexibility.

The risks and benefits should be carefully considered for each patient before use of the Zenith Alpha Thoracic Endovascular Graft. Additional considerations for patient selection include, but are not limited to:

- Patient's age and life expectancy
- Comorbidities (e.g., cardiac, pulmonary, or renal insufficiency prior to surgery, morbid obesity)
- Patient's suitability for open surgical repair
- The risk of thoracic lesion rupture compared to the risk of treatment with the Zenith Alpha Thoracic Endovascular Graft
- Ability to tolerate general, regional, or local anesthesia
- Ability and willingness to undergo and comply with the required follow-up
- Iliofemoral access vessel size and morphology (thrombus, calcification and/or tortuosity) should be compatible with vascular access techniques and accessories of the delivery profile of a 16 French (6 mm OD) to 20 French (7.7 mm OD) vascular introducer sheath
- Vascular morphology suitable for endovascular repair, including:
  - Radius of curvature greater than or equal to 20 mm along the entire length of aorta intended to be treated.
- Nonaneurysmal aortic segments (fixation sites) proximal and distal to the thoracic lesion:
  - with a length of at least 20 mm,
  - with a diameter measured outer-wall-to-outer-wall of no greater than 42 mm and no less than 15 mm, and with localized angulations less than 45 degrees.

The final treatment decision is at the discretion of the physician and patient.

8 PATIENT COUNSELING INFORMATION

The physician and patient (and/or family members) should review the risks and benefits when discussing this endovascular device and procedure, including:

- Risks and differences between endovascular repair and open surgical repair
- Potential advantages of traditional open surgical repair
- Potential advantages of endovascular repair
- The possibility that subsequent interventional or open surgical repair of the thoracic lesion may be required after initial endovascular repair.

In addition to the risks and benefits of an endovascular repair, the physician should assess the patient's commitment to and compliance with postoperative follow-up as necessary to ensure continuing safe and effective results. Listed below are additional topics to discuss with the patient as to expectations after an endovascular repair:

- **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcer, or changes in the structure or position of the endovascular graft) should receive enhanced follow-up. Specific follow-up guidelines are described in **Section 12, IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP.**
- Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be told that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of thoracic aortic lesions. At a minimum, annual imaging and adherence to routine postoperative follow-up requirements is required and should be considered a life-long commitment to the patient's health and well-being.
- The patient should be told that successful thoracic lesion repair does not arrest the disease process. It is still possible to have associated degeneration of vessels.
- Physicians must advise every patient that it is important to seek prompt medical attention if he/she experiences signs of graft occlusion, thoracic lesion enlargement or rupture. Signs of graft occlusion include, but may not be limited to, pulse-less legs, ischemia of intestines, and cold extremities. Thoracic lesion rupture may be asymptomatic, but usually presents as back or chest pain, persistent cough, dizziness, fainting, rapid heartbeat, or sudden weakness.
- Due to the imaging required for successful placement and follow-up of endovascular devices, the risk of radiation exposure to developing tissue should be discussed with women who are or suspect they are pregnant.
- Men who undergo endovascular or open surgical repair may experience impotence.

The physician should complete the Patient ID Card and give it to the patient so that he/she can carry it with him/her at all times. The patient should refer to the card any time he/she visits additional health practitioners, particularly for any additional diagnostic procedures (e.g., MRI).

9 HOW SUPPLIED

- The Zenith Alpha Thoracic Endovascular Graft is sterilized by ethylene oxide gas, is preloaded onto an introduction system, and is supplied in peel-open packages.
- The device is intended for single use only. Do not resterilize the device.
- The product is sterile if the package is unopened and undamaged. Inspect the device and packaging to verify that no damage has occurred as a result of shipping. Do not use this device if damage has occurred or if the sterilization barrier has been damaged or broken. If damage has occurred, do not use the product; instead, return the product to Cook.
- Prior to use, verify that the correct devices (quantity and size) have been supplied for the patient by matching the device to the order prescribed by the physician for that particular patient.
- The device is loaded into a 16 French, 18 French or 20 French Flexor Introducer Sheath. Its surface is treated with a hydrophilic coating that, when hydrated, enhances trackability. To activate the hydrophilic coating, the surface must be wiped with a sterile gauze pad soaked in saline solution under sterile conditions.
- Do not use after the expiration date printed on the label.
- Store in a dark, cool, dry place.

10 CLINICAL USE INFORMATION

10.1 Physician Training

CAUTION: Always have a qualified surgery team available during implantation or reintervention procedures in the event that conversion to open surgical repair is necessary.

CAUTION: The Zenith Alpha Thoracic Endovascular Graft should only be used by physicians and teams trained in vascular interventional techniques (endovascular and surgical) and in the use of this device. The recommended skill and knowledge requirements for physicians using the Zenith Alpha Thoracic Endovascular Graft are outlined below:

Patient Selection

- Knowledge of the natural history of thoracic aortic lesions (aneurysms, ulcers, or blunt thoracic aortic injury) and comorbidities associated with thoracic aortic lesion repair.
- Knowledge of radiographic image interpretation, patient selection, device selection, planning, and sizing.

A multidisciplinary team that has combined procedural experience with:

- Femoral and brachial cutdown, arteriotomy, and repair or conduit technique
- Percutaneous access and closure techniques
- Nonselective and selective wire guide and catheter techniques
- Fluoroscopic and angiographic image interpretation
- Embolization
- Angioplasty
- Endovascular stent placement
- Snare techniques
- Appropriate use of radiographic contrast material
- Techniques to minimize radiation exposure
- Expertise in necessary patient follow-up modalities

10.2 Inspection Prior to Use

Inspect the device and packaging to verify that no damage has occurred as a result of shipping. Do not use this device if damage has occurred or if the sterilization barrier has been damaged or broken. If damage has occurred, do not use the product; instead, return the product to Cook. Prior to use, verify correct devices (quantity and size) have been supplied for the patient by matching the device to the order prescribed by the physician for that particular patient.

10.3 Materials Required

(Not included in the endovascular graft system)

- A selection of Zenith Alpha Thoracic Endovascular Graft distal ancillary components in diameters compatible with the proximal and distal components.
- Fluoroscope with digital angiography capabilities (C-arm or fixed unit)
- Contrast media
- Power injector
- Syringe
- Heparinized saline solution
- Sterile gauze pads

10.4 Materials Recommended

The following products are recommended for implantation of any component in the Zenith product line. For information on the use of these products, refer to the individual product's **Suggested Instructions for Use**:

- .035 inch (0.89 mm) extra stiff wire guide, 260/300 cm:
  - Cook Lunderquist Extra Stiff Wire Guides (LESDC)
  - Cook Amplatz Ultra Stiff Wire Guides (AUS)
- .035 inch (0.89 mm) standard wire guide:
  - Cook .035 inch Wire Guides
  - Cook .035 inch Bentson Wire Guide
  - Cook Nimble® Wire Guides
- Molding balloons:
  - Cook Coda® Balloon Catheters
- Introducer sets:
  - Cook Check-Flo® Introducer Sets
- Sizing catheter:
  - Cook Aurous® Centimeter Sizing Catheters
- Angiographic radiopaque marker catheters:
  - Cook Beacon® Tip Angiographic Catheters
  - Cook Beacon® Tip Royal Flush Catheters, 125 cm
- Entry needles:
  - Cook single wall entry needles
- Endovascular dilators:
  - Cook endovascular dilator sets

10.5 Device Diameter Sizing Guidelines

The choice of diameter should be determined from the outer-wall-to-outer-wall vessel diameter and **not** the lumen diameter. Undersizing (as observed during the clinical studies; refer to the Device Performance sections in the SUMMARY OF CLINICAL DATA) or oversizing may result in incomplete sealing or compromised flow. In order to ensure accurate diameter measurements for the purpose of graft sizing, particularly when in curved segments of the aorta, measure the aortic diameter using 3D reconstructed views perpendicular to the aortic centerline of flow. The proximal diameter of the distal component can be up to 8 mm larger in diameter than the distal diameter of the proximal component. It is strongly recommended that you ensure a minimum three-stent overlap between components.

For patients with blunt thoracic aortic injuries, if there is significant periaortic hematoma in the region of the subclavian artery the hematoma should not be counted in the diameter measurement, as there is a risk of oversizing the graft. For blunt thoracic aortic injury patients, CTA measurements should be based on a CTA of a fully resuscitated patient.

Table 1 – Proximal, Distal and Proximal Tapered Component (P, D, PT) Graft Diameter Sizing Guide*

Intended Aortic Vessel Diameter[1,2] (mm)	Graft Diameter[3] (mm)	Overall Length of Proximal Component (mm)	Overall Length of Distal Component (mm)	Overall Length of Tapered Proximal Component (mm)	Introducer Sheath (Fr)	Introducer Sheath Outer Diameter (OD) (mm)
15	18	105/127**	n/a	n/a	16	6.0
16	18	105/127**	n/a	n/a	16	6.0
17	20	105/127**	n/a	n/a	16	6.0
18	22	105/127**	n/a	105**	16	6.0
19	22	105/127**	n/a	105**	16	6.0
20	24	105/127**	n/a	n/a	16	6.0
21	24	105/127**	n/a	n/a	16	6.0
22	26	105/149**	n/a	105	16	6.0
23	26	105/149**	n/a	105	16	6.0
24	28	109/132**/155/201	160/229**	n/a	16	6.0
25	28	109/132**/155/201	160/229**	n/a	16	6.0
26	30	109/132**/155/201	160/229**	108	16	6.0
27	30	109/132**/155/201	160/229**	108	16	6.0
28	32	109/132**/155/201	160/229**	178/201	18	7.1
29	32	109/132**/155/201	160/229**	178/201	18	7.1
30	34	113/137**/161/209	142/190	161/209	18	7.1
31	36	113/137**/161/209	142/190	161/209	18	7.1
32	36	113/137**/161/209	142/190	161/209	18	7.1
33	38	117/142**/167/217	147/197	167/217	18	7.1
34	38	117/142**/167/217	147/197	167/217	18	7.1
35	40	117/142**/167/217	147/197	167/217	20	7.7
36	40	117/142**/167/217	147/197	167/217	20	7.7
37	42	121/147**/173/225	152**/204	173/225	20	7.7
38	42	121/147**/173/225	152**/204	173/225	20	7.7
39	44	125/152**/179/233	157**/211	179/233	20	7.7
40	46	125/152**/179/233	157**/211	179/233	20	7.7
41	46	125/152**/179/233	157**/211	179/233	20	7.7
42	46	125/152**/179/233	157**/211	179/233	20	7.7

*All dimensions are nominal.

**Non stock items.

[1] Maximum diameter along the fixation site, measured outer-wall-to-outer-wall.

[2] Round the measured aortic diameter to the nearest mm.

[3] Additional considerations may affect the choice of diameter.

Table 2 – Distal Extension (DE) Graft Diameter Sizing Guide*

Intended Aortic Vessel Diameter[1,2] (mm)	Graft Diameter[3] (mm)
15	18
16	18
17	20
18	22
19	22
20	24
21	24
22	26
23	26
24	28
25	28
26	30
27	30
28	32
29	32
30	34
31	36
32	36
33	38
34	38
35	40
36	40
37	42
38	42
39	44
40	46
41	46
42	46

*All dimensions are nominal.
**Non stock items.
[1] Maximum diameter along the fixation site, measured outer-wall-to-outer-wall.
[2] Round the measured aortic diameter to the nearest mm.
[3] Additional considerations may affect the choice of diameter.

10.6 Device Length Sizing Guidelines

- Graft length should be selected to cover the lesion as measured along the greater curve of the aneurysm, plus a minimum of 20 mm of seal zone on the proximal and distal ends.
- To treat more focal aortic injuries, as often found in blunt thoracic aortic injury patients, a proximal component can be used alone.
- In aneurysms the graft may settle into the greater curve of the aneurysm over time. Accordingly, extra graft length needs to be planned.
  - A two-component repair (proximal and distal component) is recommended, as it provides the ability to adapt to the length change over time. A two-component repair (proximal and distal component) also provides active fixation at both the proximal and distal seal sites.
  - The minimum required amount of overlap between devices is three stents. Less than a three-stent overlap may result in endoleak (with or without component separation). However, no part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall. Device lengths should be selected accordingly.
  - If an acceptable two-component (proximal and distal component) treatment plan cannot be achieved (e.g., excessive aortic coverage, even with maximal overlap of shortest components), the proximal component must be selected with enough length to achieve and maintain the minimum 20 mm sealing zones at both ends even when positioned in the greater curve of the aneurysm. Failure to do so could result in migration, endoleak, and aneurysm growth, as observed in the clinical study (refer to the Device Performance section in the SUMMARY OF CLINICAL DATA from the aneurysm/ulcer study).

11 DIRECTIONS FOR USE

Anatomical Requirements

- Iliofemoral access vessel size and morphology (minimal thrombus, calcium and/or tortuosity) should be compatible with vascular access techniques and accessories. Arterial conduit technique may be required.
- Proximal and distal aortic neck lengths should be a minimum of 20 mm.
- Aortic neck diameters measured outer-wall-to-outer-wall should be between 15-42 mm.
- A proximal neck diameter that is 4 mm or more larger than the distal neck diameter requires the use of a proximal tapered component.
- No localized angulation should be larger than 45 degrees.
- Measurements to be taken during the pretreatment assessment are shown in **Fig. 3** and **Fig. 4.**

Proximal and Distal Component Overlap

A minimum overlap of three stents is recommended; however, the proximal sealing stent of the proximal component or distal sealing stent of the distal component should not be overlapped.

Prior to use of the Zenith Alpha Thoracic Endovascular Graft, review the Suggested Instructions for Use booklet. The following instructions are intended to help guide the physician and do not take the place of physician judgment.

General Use Information

Standard techniques for placement of arterial access sheaths, guiding catheters, angiographic catheters, and wire guides should be employed during use of the Zenith Alpha Thoracic Endovascular Graft. The Zenith Alpha Thoracic Endovascular Graft is compatible with .035 inch diameter wire guides. Brachio-femoral wire guide technique may be required if the patient has a difficult anatomy.

Endovascular stenting is a surgical procedure, and blood loss from various causes may occur, infrequently requiring intervention (including transfusion) to prevent adverse outcomes. It is important to monitor blood loss from the hemostatic valve throughout the procedure, but is specifically relevant during and after manipulation of the gray positioner. After the gray positioner has been removed, if blood loss is excessive, consider placing an uninflated molding balloon or an introduction system dilator within the valve to restrict flow.

Pre-Implant Determinants

Verify from pre-implant planning that the correct device has been selected. Determinants include:

- Femoral artery selection for introduction of the introduction system(s)
- Angulation of aorta, aneurysm, and iliac arteries
- Quality of the proximal and distal fixation sites
- Diameters of proximal and distal fixation sites and distal iliac arteries
- Length of proximal and distal fixation sites

Patient Preparation

1. Refer to institutional protocols relating to anesthesia, anticoagulation, and monitoring of vital signs.
2. Position the patient on the imaging table to allow fluoroscopic visualization from the aortic arch to the femoral bifurcations.
3. Expose the femoral artery using standard surgical technique.
4. Establish adequate proximal and distal vascular control of the femoral artery.

11.1 The Zenith Alpha Thoracic Endovascular Graft

11.1.1 Proximal and Distal Components Preparation/Flush

1. Remove the yellow-hubbed inner stylet from the dilator tip. Verify that the Captor Sleeve is within the Captor Hemostatic Valve; do not remove the Captor Sleeve. (**Fig. 5**)
2. Elevate the distal tip of the system and flush through the hemostatic valve until fluid exits the tip of the introducer sheath. (**Fig. 6**) Continue to inject a further 10 ml of flushing solution through the device. Discontinue injection and close the stopcock on the connecting tube.
   NOTE: Graft flushing solution of heparinized saline is often used.
3. Attach a syringe with heparinized saline to the hub on the rotation handle. (**Fig. 7**) Flush until fluid exits the distal sideports and dilator tip.
4. Soak sterile gauze pads in saline solution and use them to wipe the Flexor Introducer Sheath to activate the hydrophilic coating. Hydrate both sheath and dilator tip liberally.

11.1.2 Placement of Proximal Component

1. Puncture the selected artery using standard technique with an 18-gage access needle. Upon vessel entry, insert:
   - Wire guide – standard .035 inch, 260/300 cm, 15 mm J tip or Benson wire guide.
   - Appropriate size sheath (e.g., 5 French).
   - Pigtail flush catheter (often radiopaque-banded sizing catheters; e.g., Cook Centimeter Sizing CSC-20 catheter).
2. Perform angiography at the appropriate level. If using radiopaque markers, adjust position of the catheter as necessary and repeat angiography.
3. Ensure the graft system has been flushed and primed with heparinized saline (appropriate flush solution), and all air has been removed.
4. Give systemic heparin. Flush all catheters and wet all wire guides with heparinized saline. Reflush catheters and rewet wire guides after each exchange.
5. Replace the standard wire guide with a stiff .035 inch, 260/300 cm, LESDC wire guide and advance through the catheter and up to the aortic arch.
   NOTE: If the anatomy is difficult, consider using a brachio-femoral approach instead.
6. Remove the pigtail flush catheter and sheath.
   NOTE: At this stage, the second femoral artery can be accessed for angiographic catheter placement. Alternatively, consider using a brachial approach.
7. Introduce the freshly hydrated introduction system over the wire guide and advance it until the desired graft position is reached.
   CAUTION: To avoid inadvertent displacement of the graft during withdrawal of the sheath, it may be appropriate to momentarily decrease the patient's mean arterial pressure to approximately 80 mm Hg (at the discretion of the physician).
   CAUTION: To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.
   NOTE: The dilator tip will soften at body temperature.
8. Verify wire guide position in the aortic arch. Ensure correct graft position.
   CAUTION: Care should be taken not to advance the sheath while the stent graft is still within it. Advancing the sheath at this stage may cause the barbs to perforate the introducer sheath.
9. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned to the open position. (**Fig. 8**)
10. Stabilize the gray positioner (introduction system shaft) and withdraw the sheath until the graft is fully expanded and the valve assembly with the Captor Sleeve docks with the black gripper. (**Fig. 9**)
    CAUTION: As the sheath is withdrawn, anatomy and graft position may change. Prior to complete unsheathing of the graft, check distal gold markers to make sure visceral arteries will not be covered. Constantly monitor graft position and perform angiography to check position as necessary.
    CAUTION: During sheath withdrawal, the proximal barbs are exposed and are in contact with the vessel wall. At this stage it may be possible to advance the device, but retraction may cause aortic wall damage.
    NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.
11. Verify graft position and, if necessary, adjust it forward. Recheck graft position with angiography.
    NOTE: If an angiographic catheter is placed parallel to the stent graft, use this to perform position angiography.
12. While holding the black gripper, turn the black safety-lock knob in the direction of the arrows to engage the blue rotation handle. (**Fig. 10**) Make sure the black safety-lock knob is in the unlocked position.
13. Under fluoroscopy, turn the blue rotation handle in the direction of the arrow until a stop is felt. (**Fig. 11**) This indicates that the uncovered stent and proximal end of the graft have opened and that the distal attachment to the introducer has been released.
    NOTE: If the blue rotation handle stops before completing the rotation (so that the proximal end of the graft is not released from the introduction system), verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.
    NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation

handle will remain engaged. Continue with the procedure.

NOTE: If it is still difficult to rotate the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

14. Remove the introduction system, leaving the wire guide in the graft.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

NOTE: Inaccuracies in device size selection or placement, changes or anomalies in patient anatomy, or procedural complications may require placement of additional endovascular grafts and extensions to achieve the minimum length of proximal and distal seal and length of overlap between components.

11.1.3 Placement of Distal Component

1. If an angiographic catheter is placed in the femoral artery, it should be repositioned to demonstrate the aortic anatomy where the distal component is to be deployed.
2. Introduce the freshly hydrated introduction system over the wire guide until the desired graft position is reached, with at minimum a three-stent overlap (75 mm) with the proximal component. No part of the distal component should overlap the proximal sealing stent of the proximal component, and no part of the proximal component should overlap the distal sealing stent of the distal component, as doing so may cause malapposition to the vessel wall.
3. Check the graft position by angiography and adjust if necessary.
4. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned to the open position. (**Fig. 8**)
5. Stabilize the gray positioner (introduction system shaft) and begin withdrawing the sheath.

CAUTION: As the sheath is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check position as necessary.

NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.

6. Withdraw the sheath until the graft is fully expanded. Continue to withdraw the sheath until the valve assembly with the Captor Sleeve docks with the telescoping black gripper. (**Fig. 12**)
7. To release the distal attachment, hold the black gripper and turn the black safety-lock knob on the rotation handle in the direction of the arrow. Make sure the black safety-lock knob is in the unlocked position. (**Fig. 13**) Turn the blue rotation handle in the direction of the arrow next to label 1 until a stop is felt. (**Fig. 14**)

NOTE: If the blue rotation handle stops before completing the rotation, verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.

NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation handle will remain engaged. Continue with the procedure.

8. Turn the gray safety-lock knob, indicated by label 2, on the black sliding gripper in the direction of the arrow. (**Fig. 15**)

NOTE: Care should be taken to avoid landing the bare stent in regions of localized angulation > 45 degrees. If the bare stent is landed in localized angulations > 45 degrees, it may be difficult to release the bottom cap, as observed in the clinical study. Using a brachio-femoral wire guide technique can increase support of the system and ease the release of the bottom cap.

9. To release the distal bare stent, stabilize the introduction system and slide the black sliding gripper over the gray tube and outer sheath in a distal direction until it locks automatically into position next to the blue rotation handle. (**Fig. 16**) The release window on the handle next to label 3 will turn green. (**Fig. 17**) If the window has not turned green, slide the black sliding gripper until it locks with the blue rotation handle.
10. If the bare stent cannot be fully released from the cap, complete the deployment procedure and refer to **Section 13, RELEASE TROUBLESHOOTING**.
11. Turn the blue rotation handle in the direction of the arrow next to label 3 until a stop is felt and the proximal end of the graft opens.

If difficulty is encountered rotating the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

12. Remove the inner introduction system entirely, leaving the sheath and wire guide in place.
13. Close the Captor Hemostatic Valve on the Flexor Introducer Sheath by turning it to the closed position.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

11.1.4 Main Body Molding Balloon Insertion – Optional

1. Prepare the molding balloon as follows and/or per the manufacturer's instructions:
   - Flush the wire lumen with heparinized saline.
   - Remove all air from the balloon.
2. In preparation for insertion of the molding balloon, open the Captor Hemostatic Valve by turning it to the open position. (**Fig. 8**)
3. Advance the molding balloon over the wire guide and through the hemostatic valve of the main body introduction system to the level of the proximal fixation seal site. Maintain proper sheath positioning.
4. Tighten the Captor Hemostatic Valve around the molding balloon with gentle pressure by turning it to the closed position.

CAUTION: Do not inflate balloon in the aorta outside of the graft.

5. Expand the molding balloon with diluted contrast media (as directed by the manufacturer) in the area of the proximal covered stent, starting proximally and working in the distal direction.

CAUTION: Confirm complete deflation of balloon prior to repositioning.

6. If applicable, withdraw the molding balloon to the proximal component/ distal component overlap and expand.
7. Withdraw the molding balloon to the distal fixation site and expand.
8. Open the Captor Hemostatic Valve, remove the molding balloon and replace it with an angiographic catheter to perform completion angiograms.
9. Tighten the Captor Hemostatic Valve around the angiographic catheter with gentle pressure by turning it clockwise.
10. Remove or replace all stiff wire guides to allow the aorta to resume its natural position.

11.1.5 Final Angiogram

1. Position angiographic catheter just above the level of the endovascular graft. Perform angiography to verify correct positioning of the graft. Verify patency of arch vessels and celiac plexus.
2. In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers are positioned to provide adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.

NOTE: If endoleaks or other problems are observed (e.g., inadequate seal length or overlap length), refer to **Section 11.2, Ancillary Devices: Distal Extensions.**

3. Remove the sheaths, wires, and catheters.
4. Repair vessels and close in standard surgical fashion.

11.2 Ancillary Devices: Distal Extensions

General Use Information

Inaccuracies in device size selection or placement, changes or anomalies in patient anatomy, or procedural complications can require placement of additional endovascular grafts and extensions. Regardless of the device placed, the basic procedure(s) will be similar to the maneuvers required and described previously in this document. It is vital to maintain wire guide access.

Standard techniques for placement of arterial access sheaths, guiding catheters, angiographic catheters, and wire guides should be employed during use of the Zenith Alpha Thoracic Endovascular Graft ancillary devices.

The Zenith Alpha Thoracic Endovascular Graft ancillary devices are compatible with .035 inch diameter wire guides. Additional proximal main body components may be used to extend graft coverage proximally. Distal extensions are used to extend the distal body of an in situ endovascular graft or to increase the length of overlap between graft components.

11.2.1 Distal Extension Preparation/Flush

1. Remove the yellow-hubbed inner stylet from the dilator tip. Verify that the Captor Sleeve is within the Captor Hemostatic Valve; do not remove the Captor Sleeve. (**Fig. 5**)
2. Elevate distal tip of system and flush through the hemostatic valve until fluid exits the tip of the introducer sheath. (**Fig. 6**) Continue to inject a full 60 mL of flushing solution through the device. Discontinue injection and close the stopcock on the connecting tube.

NOTE: Graft flushing solution of heparinized saline is often used.

3. Attach a syringe with heparinized saline to the hub on the rotation handle. (**Fig. 7**) Flush until fluid exits the distal sideports and dilator tip.
4. Soak sterile gauze pads with saline and use to wipe the Flexor Introducer Sheath to activate the hydrophilic coating. Hydrate both sheath and dilator liberally.

11.2.2 Placement of the Distal Extension

1. Puncture the selected artery using standard technique with an 18 gage access needle. Alternatively, use the in situ wire guide that was used previously for introduction system/graft insertions. Upon vessel entry, insert:
   - Wire guide – standard .035 inch, 260/300 cm, 15 mm J tip or Bentson wire guide
   - Appropriate size sheath (e.g., 5 French)
   - Pigtail flush catheter (often radiopaque-banded sizing catheters; e.g., Cook Centimeter Sizing CSC-20 catheter
2. Perform angiography at the appropriate level. If using radiopaque markers, adjust position as necessary and repeat angiography.
3. Ensure the graft system has been primed with heparinized saline, and all air has been removed.
4. Give systemic heparin. Flush all catheters and wire guides with heparinized saline. Reflush catheters and rewet wire guides after each exchange.
5. Replace the standard wire guide with a stiff .035 inch, 260/300 cm, LESDC wire guide and advance it through the catheter and up to the aortic arch.
6. Remove the pigtail flush catheter and sheath.

NOTE: At this stage, the second femoral artery can be accessed for flush catheter placement. Alternatively, consider using a brachial approach.

7. Introduce the freshly hydrated introduction system over the wire guide and advance until the desired graft position is reached. Ensure that the distal extension overlaps the distal component by a minimum of three stents (plus the distal uncovered stent).

CAUTION: To avoid twisting the endovascular graft, never rotate the introduction system during the procedure. Allow the device to conform naturally to the curves and tortuosity of the vessels.

NOTE: The dilator tip softens at body temperature.

NOTE: To facilitate introduction of the wire guide into the introduction system, it may be necessary to slightly straighten the introduction system dilator tip.

8. Verify wire guide position in the aortic arch. Ensure correct graft position.
9. Ensure that the Captor Hemostatic Valve on the Flexor Introducer Sheath is turned counterclockwise to the open position. (**Fig. 8**)
10. Stabilize the gray positioner (introduction system shaft) and withdraw the sheath until the graft is fully expanded and the valve assembly with the Captor Sleeve docks with the black gripper. (**Fig. 9**)

CAUTION: As the sheath or wire guide is withdrawn, anatomy and graft position may change. Constantly monitor graft position and perform angiography to check position as necessary.

NOTE: If extreme difficulty is encountered when attempting to withdraw the sheath, place the device in a less tortuous position that enables the sheath to be retracted. Very carefully withdraw the sheath until it just begins to retract, and stop. Move back to original position and continue deployment.

11. Verify graft position and, if necessary, adjust it forward. Recheck graft position with angiography.
12. While holding the black gripper, turn the black safety-lock knob in the direction of the arrow to engage the blue rotation handle. (**Fig. 10**) Make sure the black safety-lock knob is in the unlocked position.
13. Under fluoroscopy, turn the blue rotation handle in the direction of the arrow until a stop is felt. (**Fig. 11**) This indicates that the proximal end of the graft has opened, and that the distal attachment to the introducer has been released.

NOTE: If the blue rotation handle stops before completing the rotation, verify the position of the black safety-lock knob and, if necessary, turn it counterclockwise to the unlock position.

NOTE: If the black safety-lock knob is removed from the system after it has been turned counterclockwise to the unlock position, the blue rotation handle will remain engaged. Continue with the procedure.

NOTE: If difficulty is still encountered during rotating the blue rotation handle, refer to **Section 13, RELEASE TROUBLESHOOTING** for instructions on how to disassemble the rotation handle.

14. Remove the inner introduction system entirely, leaving the sheath and wire guide in place.

CAUTION: To avoid entangling any catheters left in situ, rotate the introduction system during withdrawal.

15. Close the Captor Hemostatic Valve on the Flexor Introducer Sheath by turning it in a clockwise direction until it stops.

11.2.3 Distal Extension Molding Balloon Insertion – Optional

1. Prepare the molding balloon as follows and/or per the manufacturer's instructions:
   - Flush the wire lumen with heparinized saline.
   - Remove all air from the balloon.
2. In preparation for insertion of the molding balloon, open the Captor Hemostatic Valve by turning it counterclockwise. (**Fig. 8**)
3. Advance the molding balloon over the wire guide and through the Captor

Hemostatic Valve of the introduction system to the level of the distal component/distal extension overlap. Maintain proper sheath positioning.

4. Tighten the Captor Hemostatic Valve around the molding balloon with gentle pressure by turning it clockwise.
   CAUTION: Do not inflate balloon in the aorta outside of the graft.
5. Expand the molding balloon with diluted contrast media (as directed by the manufacturer) in the area of the overlap, starting proximally and working in the distal direction.
   CAUTION: Confirm complete deflation of balloon prior to repositioning.
6. Withdraw the molding balloon to the distal fixation site and expand.
7. Loosen the Captor Hemostatic Valve, remove the molding balloon and replace it with an angiographic catheter to perform completion angiograms.
8. Tighten the Captor Hemostatic Valve around the angiographic catheter with gentle pressure by turning it clockwise.
9. Remove or replace all stiff wire guides to allow aorta to resume its natural position.

11.2.4 Final Angiogram

1. Position angiographic catheter just above the level of the endovascular graft. Perform angiography to verify correct positioning. Verify patency of arch vessels and celiac plexus.
2. In the final angiogram confirm that there are no endoleaks or kinks, that the proximal and distal gold radiopaque markers are positioned to provide adequate overlap between components, and that there is sufficient graft length to maintain over time a minimum of 20 mm in proximal and distal seal.
   NOTE: If endoleaks or other problems are observed (e.g., inadequate seal length or overlap length), refer to **Section 11.2, Ancillary Devices: Distal Extensions.**
3. Remove the sheaths, wires, and catheters.
4. Repair vessels and close in standard surgical fashion.

12 IMAGING GUIDELINES AND POSTOPERATIVE FOLLOW-UP

12.1 General

- **The long-term performance of endovascular grafts has not yet been established. All patients should be advised that endovascular treatment requires life-long, regular follow-up to assess their health and the performance of their endovascular graft.** Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the endovascular graft) should receive additional follow-up. Patients should be counseled on the importance of adhering to the follow-up schedule, both during the first year and at yearly intervals thereafter. Patients should be told that regular and consistent follow-up is a critical part of ensuring the ongoing safety and effectiveness of endovascular treatment of thoracic lesions.
- Physicians should evaluate patients on an individual basis and prescribe their follow-up relative to the needs and circumstances of each individual patient. The recommended imaging schedule is presented in **Table 3**. This schedule continues to be the minimum requirement for patient follow-up and should be maintained even in the absence of clinical symptoms (e.g., pain, numbness, weakness). Patients with specific clinical findings (e.g., endoleaks, enlarging aneurysms or ulcers, or changes in the structure or position of the stent graft) should receive follow-up at more frequent intervals.
- Annual imaging follow-up should include thoracic device radiographs and both contrast and non-contrast CT examinations. If renal complications or other factors preclude the use of image contrast media, thoracic device radiographs and non-contrast CT may be used in combination with transesophageal echocardiography for assessment of endoleak.
- The combination of contrast and non-contrast CT imaging provides information on device migration, aneurysm diameter or ulcer depth change, endoleak, patency, tortuosity, progressive disease, fixation length, and other morphological changes.
- The thoracic device radiographs provide information on device migration and device integrity (separation between components, stent fracture, and barb separation) that may or may not be visible on CT depending on the quality of the scan.

Table 3 lists the minimum requirements for imaging follow-up for patients with the Zenith Alpha Thoracic Endovascular Graft. Patients requiring enhanced follow-up should have interim evaluations.

Table 3 – Recommended Imaging Schedule for Endograft Patients

	Angiogram	CT (contrast and non-contrast)	Thoracic Device Radiographs
Pre-procedure		X[1]	
Procedural	X		
1 month		X[2]	X
6 month		X[2]	X
12 month (annually thereafter)		X[2]	X

[1] Imaging should be performed within 6 months before the procedure.

[2] MR imaging may be used for those patients experiencing renal failure of who are otherwise unable to undergo contrast-enhanced CT, with transesophageal echocardiography being an additional option in the event of suboptimal MR imaging. For Type I or III endoleak, prompt intervention and additional follow-up post-intervention is recommended. See **Section 12.5, Additional Surveillance and Treatment**.

12.2 Contrast and Non-Contrast CT Recommendations

- Image sets should include all sequential images at lowest possible slice thickness (≤ 3 mm). Do NOT perform large slice thickness (> 3 mm) and/or omit consecutive CT image sets, as it prevents precise anatomical and device comparisons over time
- The same scan parameters (i.e., spacing, thickness, and FOV) should be used at each follow-up. Do not change the scan table x- or y- coordinates while scanning.
- Sequences must have matching or corresponding table positions. It is important to follow acceptable imaging protocols during the CT exam. **Table 4** lists examples of acceptable imaging protocols.

Table 4 – Acceptable Imaging Protocols

	Non-contrast	Contrast
IV contrast	No	Yes
Acceptable machines	Spiral CT or high performance MDCT capable of > 40 seconds	Spiral CT or high performance MDCT capable of > 40 seconds
Injection volume	n/a	Per institutional protocol
Injection rate	n/a	> 2.5 mL/sec
Injection mode	n/a	Power
Bolus timing	n/a	Test bolus: Smart Prep, C.A.R.E. or equivalent
Coverage - start	Neck	Subclavian aorta Coverage
- finish	Diaphragm	Profunda femoris origin
Collimation	< 3 mm	< 3 mm
Reconstruction	2.5 mm throughout - soft algorithm	2.5 mm throughout - soft algorithm
Axial DFOV	32 cm	32 cm
Post-injection runs	None	None

12.3 Thoracic Device Radiographs

The following films are required: supine-frontal (AP), cross-table lateral, 30 degree RPO, and 30 degree LPO.

Follow the following protocols during each examination:

- Record the table-to-film distance and use the same distance at each subsequent examination.
- Ensure entire device is captured on each single image format lengthwise.
- The middle photocell, thoracic spine technique, or manual technique should be used for all views to ensure adequate penetration of the mediastinum.

If there is any concern about the device integrity (e.g., kinking, stent breaks, barb separation, relative component migration), it is recommended to use magnified views. The attending physician should evaluate films for device integrity (entire device length, including components) using 2-4x magnification visual aid.

Mail:	MedicAlert Foundation International 2323 Colorado Avenue Turlock, CA 95382
Phone:	888-633-4298 (toll free) 209-668-3333 from outside the US
Fax:	209-669-2450
Web:	www.medicalert.org

12.4 MRI Safety Information

Nonclinical testing has demonstrated that the Zenith Alpha Thoracic Endovascular Graft is MR Conditional according to ASTM F2503. A patient with this endovascular graft can be scanned safely after placement under the following conditions.

- Static magnetic field of 1.5 or 3.0 tesla.
- Maximum spatial magnetic field of 1600 gauss/cm (16.0 T/m)or less
- Maximum MR system reported, whole-body-averaged specific absorption rate (SAR) of ≤ 2 W/kg (normal operating mode) for 15 minutes of continuous scanning

Under the scan conditions defined above, the Zenith Alpha Thoracic Endovascular Graft is expected to produce a maximum temperature rise of less than 2.1°C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 5 mm from the Zenith Alpha Thoracic Endovascular Graft when imaged with a gradient echo pulse sequence and a 3.0 T MR system. The image artifact obscures a portion of the device lumen.

For U.S. Patients Only

Cook recommends that the patient register the MR conditions disclosed in this IFU with the MedicAlert Foundation. The MedicAlert Foundation can be contacted in the following manners:

12.5 Additional Surveillance and Treatment

(Refer to **Section 4, WARNINGS AND PRECAUTIONS**)

Additional surveillance and possible treatment is recommended for:

- Type I endoleak
- Type III endoleak
- Aneurysm or ulcer enlargement, ≥ 5 mm of maximum aneurysm diameter or ulcer depth (regardless of endoleak status)
- Migration
- Inadequate seal length
- Graft thrombosis or occlusion
- Loss of device integrity
  - Barb separation
  - Stent fracture
  - Relative component migration

Consideration for reintervention or conversion to open repair should include the attending physician's assessment of an individual patient's comorbidities, life expectancy, and the patient's personal choices. Patients should be counseled that subsequent reinterventions, including catheter-based and open surgical conversion, are possible following endograft placement.

13 RELEASE TROUBLESHOOTING

NOTE: Technical assistance from a Cook product specialist may be obtained by contacting your local Cook representative.

13.1 Difficulty Removing Release Wires

Turning the rotation handle pulls the release wire back, releasing the stent graft attachment to the introducer. If the stent graft is not completely released, it is possible to disassemble the rotation handle by following the steps below.

1. Use surgical forceps to pull the back-end clips out (**Fig. 18** and **19**) and remove the back-end cap. (**Fig. 20**)
2. Stabilize the gray positioner and slide the blue rotation handle backward to pull the release wires until the graft is released. Do not pull the release wires completely out of the rotation handle. (**Fig. 21** and **22**)
3. If leakage thought the valve occurs, remove the inner introduction system entirely, leaving the sheath and wire guide in place.
4. Close the Captor Hemostatic Valve on the Flexor introducer sheath by turning it to the closed position.

   NOTE: If extreme force is needed, wind the release wires around the surgical forceps. (**Fig. 23**)

13.2 Distal Component - Bare Stent Deployment

If the bare stent cannot be fully deployed from the cap: (**Fig. 24**)

1. Advance the Flexor sheath to the distal edge of the stent graft. (**Fig. 25** and **26**)
2. Stabilize the Flexor sheath and pull back the blue rotation handle. (**Fig. 27**)

The bare stent will now be released from the cap but still be inside the sheath. Withdraw the sheath **SLOWLY** with a rotating movement (**Fig. 28**) until the bare stent is outside the sheath.

Manufacturer
WILLIAM COOK EUROPE ApS
Sandet 6, DK-4632
Bjaeverskov, DENMARK

www.cookmedical.com

2015-02
I-ALPHA-THORACIC-438-0

6. Summary of Clinical Data

The Zenith Alpha™ Thoracic Endovascular Graft is indicated for the endovascular treatment of patients with isolated lesions of the descending thoracic aorta (not including dissections) having vascular anatomy suitable for endovascular repair.

The Zenith Alpha™ Thoracic Endovascular Graft has been the subject of several documented clinical evaluations, including two pivotal studies (one international) that evaluated the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft in patients with thoracic aneurysm/ulcer and blunt thoracic aortic injury, as summarized in Table 6-1. Additional clinical evaluations include a continued access study for the aneurysm/ulcer indication (see Section 6.3.2) and a European post-market survey (see Section 6.3.3) to further confirm performance of a user interface modification to the introduction system (rotation handle).

Table 6-1. Summary of primary pivotal studies

Pivotal Study	Study Design	Objective	Number of Sites with Enrollment	Number of Patients
Aneurysm/ Ulcer	Prospective, nonrandomized, single-arm, multinational (US, Japan, Germany, England, Sweden) study	To evaluate safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with aneurysms/ulcers of the descending thoracic aorta.	23	110
BTAI	Prospective, nonrandomized, noncomparative, single-arm, US multicenter study	To evaluate safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of BTAI	17	50

6.1. Clinical Study for the Aneurysm/Ulcer Indication

The Zenith Alpha™ Thoracic Endovascular Graft clinical study was a prospective, nonrandomized, single-arm, multinational study that was conducted to evaluate the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with aneurysms/ulcers of the descending thoracic aorta. Patients were treated between March 17, 2010 (first US enrollment on October 1, 2010) and January 16, 2013. The data presented herein was collected on 110 patients through April 7, 2015. There were 23 investigational sites, including centers in the US (51 patients at 14 sites), Japan (43 patients at 3 sites), Germany (13 patients at 4 sites), Sweden (3 patients at 1 site), and England (1 patient at 1 site). The presenting anatomy, based on core laboratory analysis

of pre-procedure imaging, was a thoracic aneurysm in 81.8% (90/110) of patients and a thoracic ulcer in 18.2% (20/110) of patients.

The pivotal study endpoints were established based on performance goals derived from the pivotal study of the previous device, the Zenith® TX2® TAA Endovascular Graft. Similar inclusion/exclusion criteria were used between the two studies. A post hoc analysis was performed comparing demographic, comorbid, and baseline anatomical characteristics between the present study and the previous Zenith® TX2® TAA Endovascular Graft study used to derive the performance goals for hypothesis testing. Of the few variables that were found to be different between studies, none appeared to be relevant with respect to assessing the safety and effectiveness endpoints, thus confirming that comparing to performance goals derived from the previous study remained appropriate.

The primary safety endpoint was 30-day freedom from major adverse events (MAEs), and the performance goal was 80.6%. MAEs were defined as the following: all-cause death; Q-wave MI; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

The primary effectiveness endpoint was device success at 12-month. Device success at 12 months was defined as: Technical Success, with none of the following at 12 months:

- Type I or type III endoleaks requiring re-intervention
- Aneurysm rupture or conversion to open surgical repair
- Aneurysm enlargement greater than 0.5 cm

Technical success was defined as successful access of the aneurysm site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location. The endovascular graft must be patent at the time of deployment completion as evidenced by intraoperative angiography.

The effectiveness hypothesis of the study was that device success at 12 months met the performance goal of 80.7%.

An independent core laboratory analyzed all patient imaging. An independent clinical events committee (CEC) adjudicated all major adverse events (MAEs), including all patient deaths; additionally the CEC also adjudicated core laboratory reports of migration and device integrity loss. An independent data safety monitoring board (DSMB) monitored the clinical trial according to an established safety monitoring plan.

The study follow-up schedule (Table 6.1-1) consisted of both clinical and imaging (CT and X-ray) assessments at post-procedure (pre-discharge), 30 days, 6 months, 12 months, and yearly thereafter through 5 years.

Table 6.1-1. Study follow-up schedule

Study Schedule							
	Pre-op	Intra-op	Post-procedure	30-Day	6-Month	12-Month	24-Month[d]
Clinical exam	X		X	X	X	X	X
Blood tests	X		X	X	X	X	X
CT scan	X[a]			X[c]	X[c]	X[c]	X[c]
Thoracic x-ray				X	X	X	X
Angiography	X[b]	X					

[a]It is recommended that imaging be performed within 6 months before the procedure.
[b]Required only to resolve any uncertainties in anatomical measurements necessary for graft sizing.
[c]MR imaging may be used for those patients experiencing renal failure or who are otherwise unable to undergo contrast-enhanced CT scan, with TEE being an additional option in the event of suboptimal MR imaging.
[d]Yearly thereafter through 5 years.

At the time of the database lock, of 110 patients enrolled in the study, 90% (99/110) were eligible for follow-up at 12 months (Table 6.1-2). All patients were evaluable for the primary safety endpoint (freedom from MAE at 30 days). All patients were also evaluable for the primary effectiveness endpoint (12-month device success) based on a component of the composite measure having been assessed at the time of the procedure, consistent with the performance goal development. Two patients, although enrolled in the study, did not receive the device due to an inability to advance/gain access to the target treatment site. Although the primary safety and effectiveness endpoints were evaluated at 30 days and 12 months, respectively, patient data presented herein include longer-term follow-up that was available at the time of the data lock (April 7, 2015). Table 6.1-2 reports the percent of follow-up data available through 4 years.

Table 6.1-2. Follow-up availability

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]				Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Patients with Data for that Visit	CT[c]	X-ray	Patients with Follow-up Pending[d]	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
Operative	110	110/110 (100%)	NA	NA	0	NA	NA	NA	NA	0	0	0	0
30-day	110[e]	106/110 (96.4%)	105/108 (97.2%)	98/108 (90.7%)	0	105/108 (97.2%)	102/108 (94.4%)	NA	105/108 (97.2%)	3	0	0	2[e]
6-month	105	99/105 (94.3%)	97/105 (92.4%)	92/105 (87.6%)	0	96/105 (91.4%)	91/105 (86.7%)	94/105 (89.5%)	98/105 (93.3%)	2	0	4	0
12-month	99	91/99 (91.9%)	92/99 (92.9%)	84/99 (84.8%)	0	92/99 (92.9%)	83/99 (83.8%)	92/99 (92.9%)	92/99 (92.9%)	7	1	2	0
2-year	89	78/89 (87.6%)	79/89 (88.8%)	75/89 (84.3%)	8	77/89 (86.5%)	73/89 (82.0%)	77/89 (86.5%)	77/89 (86.5%)	3	0	7	45
3-year	34	23/34 (67.6%)	20/34 (58.8%)	18/34 (52.9%)	11	17/34 (50.0%)	15/34 (44.1%)	17/34 (50.0%)	17/34 (50.0%)	0	0	0	26
4-year	8	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	2	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	6/8 (75.0%)	0	0	0	8

NA – Not assessed.
LTF/WTHD – Lost-to-follow-up and withdrawn.
[a]Site-submitted data.
[b]Based on core laboratory analysis.
[c]Includes MRI or TEE imaging (which is allowed per protocol) when the patient is unable to receive contrast medium due to renal failure.
[d]Patients still within follow-up window, but data not yet available.
[e]Two patients did not receive the device at the time of the implant procedure and therefore only 30-day clinical follow-up was applicable before the patients exited the study, with no further follow-up due thereafter.

Demographics and Patient Characteristics

The demographics and patient characteristics are presented in Table 6.1-3.

Table 6.1-3. Demographics and patient characteristics

Demographic	Mean ± SD (n, range) or Percent Patients (number/total number)
Age (years)	
All patients	72.2 ± 9.8 (n=110, 42 – 92)
Male	70.7 ± 9.9 (n=64, 42 – 85)
Female	74.3 ± 9.4 (n=46, 44 – 92)
Gender	
Male	58.2% (64/110)
Female	41.8% (46/110)
Ethnicity	
White	53.6% (59/110)
Hispanic or Latino	0
Black or African American	8.2% (9/110)
American Indian or Alaska Native	0
Asian	38.2% (42/110)
Native Hawaiian or other Pacific Islander	0
Other	0
Height (in)	65.3 ± 4.5 (n=110, 55.1 – 75.2)
Weight (lbs)	161.7 ± 44.3 (n=110, 79.2 – 330.0)
Body mass index	26.5 ± 6.0 (n=110, 16.4 – 50.0)

The medical history and comorbid medical conditions for the patient cohort are presented in Table 6.1-4.

Table 6.1-4. Pre-existing comorbid medical conditions

Medical History	Percent Patients (number/total number)
Cardiovascular	
Myocardial infarction (MI)	12.7% (14/110)
Angioplasty/stent	10.0% (11/110)
Cardiac or thoracic surgery	16.4% (18/110)
Prior diagnosis of symptomatic congestive heart failure (CHF)	10.0% (11/110)
Angina	16.4% (18/110)
Prior diagnosis of arrhythmia	23.6% (26/110)
Hypertension	88.2% (97/110)
Coronary artery bypass graft	11.8% (13/110)

Medical History	Percent Patients (number/total number)
Vascular	
Thromboembolic event	0.9% (1/110)
Peripheral vascular disease	21.8% (24/110)
Symptomatic carotid disease warranting intervention	1.8% (2/110)
Any aneurysm (other than the study lesion)	45.5% (50/110)
Thoracic aortic aneurysm	2.7% (3/110)
Abdominal aortic aneurysm	26.4% (29/110)
Other aneurysm[a]	16.4% (18/110)
Degenerative or atherosclerotic ulcer (other than the study lesion)	0.9% (1/110)
Any dissection	9.1% (10/110)[b]
Thoracic aortic dissection	6.4% (7/110)[c]
Abdominal aortic dissection	0
Other dissection[d]	2.7% (3/110)
Thoracic trauma	3.6% (4/110)[e]
Aortobronchial fistula	0.9% (1/110)
Aortoesophageal fistula	0
Bleeding diathesis or uncorrectable coagulopathy	0
Endarterectomy	1.8% (2/110)
Diagnosed or suspected congenital degenerative collagen disease	0
Pulmonary	
Chronic obstructive pulmonary disease (COPD)	25.5% (28/110)
Home oxygen	1.8% (2/110)
Renal	
Chronic renal failure	10.0% (11/110)
Hemodialysis	1.8% (2/110)
Chronic peritoneal dialysis	0
Endocrine	
Diabetes	19.1% (21/110)
Hypercholesterolemia	73.6% (81/110)
Infectious disease	
Systemic infection	0
Gastrointestinal	
Gastrointestinal disease	34.5% (38/110)
Hepatobiliary	
Liver disease	12.7% (14/110)
Neoplasms	
Cancer	24.5% (27/110)
Neurologic	
Stroke	10.9% (12/110)
Substance use	
Past or current smoker	71.8% (79/110)
Allergies	
Allergies	41.8% (46/110)

[a]The "other" aneurysm category includes patients with aneurysms in different locations (i.e., not descending thoracic or abdominal aorta) and patients with aneurysms in multiple locations.
[b]All patients had a history of aortic dissection but at the time of enrollment had no radiographic evidence of aortic dissection.
[c]The treated aneurysm/ulcer was located in the same aortic segment as the previously diagnosed dissection in four patients.
[d]The "other" dissection category includes patients with dissection in different locations (i.e., not descending thoracic or abdominal aorta) and patients with dissections in multiple locations.
[e]All patients had a history (> 1 year) of traumatic thoracic injury.

Table 6.1-5 reports the ASA classification.

Table 6.1-5. ASA physical status classification

ASA Classification	Percent Patients (number/total number)
Healthy patient (1)	8.2% (9/110)
Mild systemic disease (2)	55.5% (61/110)
Severe systemic disease (3)	26.4% (29/110)
Incapacitating systemic disease (4)	10.0% (11/110)
Moribund patient (5)	0

Table 6.1-6 reports the SVS-ISCVS risk score.

Table 6.1-6. SVS-ISCVS risk score classification

SVS-ISCVS Category	Percent Patients (number/total number)
Diabetes risk score	
0	83.6% (92/110)
1	5.5% (6/110)
2	9.1% (10/110)
3	1.8% (2/110)
4	0
Smoking risk score	
0	47.3% (52/110)
1	30.0% (33/110)
2	13.6% (15/110)
3	9.1% (10/110)
Hypertension risk score	
0	11.8% (13/110)
1	29.1% (32/110)
2	31.8% (35/110)
3	27.3% (30/110)
Hyperlipidemia risk score	
0	26.4% (29/110)
1	17.3% (19/110)
2	1.8% (2/110)
3	54.5% (60/110)
Cardiac status risk score	
0	70.0% (77/110)
1	18.2% (20/110)
2	11.8% (13/110)
3	0
Carotid disease risk score	
0	84.5% (93/110)
1	13.6% (15/110)
2	0.9% (1/110)
3	0.9% (1/110)

SVS-ISCVS Category	Percent Patients (number/total number)
Renal status risk score	
0	87.3% (96/110)
1	10.9% (12/110)
2	0
3	1.8% (2/110)
Pulmonary status risk score	
0	66.4% (73/110)
1	26.4% (29/110)
2	6.4% (7/110)
3	0.9% (1/110)
Total SVS/ISCVS risk score	5.9 ± 2.6 (n=110, 1 – 14)

The majority of patients (81.8%) had fusiform aneurysms and the remaining 18.2% had penetrating atherosclerotic ulcers. Table 6.1-7 reports the presenting morphology.

Table 6.1-7. Presenting morphology type per the core laboratory

Morphology	Percent Patients (number/total number)
Aneurysm	81.8% (90/110)
Ulcer	18.2% (20/110)

Table 6.1-8 reports presenting anatomical dimensions of the aneurysm/ulcer, the proximal and distal aortic necks, and the right and left iliac arteries.

Table 6.1-8. Presenting anatomical dimensions reported per the core laboratory

Measure	Mean ± SD (n, range)
Aneurysm dimensions	
Major diameter (mm)	60.9 ± 11.4 (n=90, 41 – 99)
Minor diameter (mm)	51.7 ± 11.1 (n=90, 30 – 92)
Length (mm)	113.5 ± 63.0 (n=90, 25.4 – 324.0)
Ulcer dimensions	
Ulcer depth (mm)	14.1 ± 3.7 (n=20, 8 – 25)
Length (mm)	34.8 ± 20.3 (n=20, 11.0 – 85.7)
Proximal neck diameter	
Left common carotid artery	
Major (mm)	34.0 ± 3.0 (n=110, 24 – 42)
Minor (mm)	31.1 ± 3.5 (n=110, 18 – 39)
20 mm distal to left common carotid artery	
Major (mm)	33.3 ± 4.3 (n=110, 22 – 54)
Minor (mm)	30.6 ± 4.3 (n=110, 20 – 49)
Distal neck diameter	
20 mm proximal to celiac artery	
Major (mm)	31.0 ± 5.1 (n=110, 20 – 48)
Minor (mm)	28.9 ± 4.7 (n=110, 19 – 42)
Celiac artery	
Major (mm)	29.5 ± 4.4 (n=110, 20 – 44)

Measure	Mean ± SD (n, range)
Minor (mm)	27.3 ± 3.8 (n=110, 19 – 38)
Proximal neck length Left common carotid artery to distal part of neck (mm)	94.7 ± 57.8 (n=110, 14.4 – 276.7)
Distal neck length Celiac artery to proximal part of neck (mm)	105.2 ± 63.2 (n=110, 5.6 – 268.5)
Right iliac artery diameter Narrowest segment (mm)	6.7 ± 1.6 (n=105, 3 – 10)[a]
Left iliac artery diameter Narrowest segment (mm)	6.9 ± 1.8 (n=104, 0 – 11)[a]

[a]CT imaging was not always adequate for measurement of the iliac arteries.

Table 6.1-9 reports the distribution in aneurysm diameter/ulcer depth.

Table 6.1-9. Distribution in range of maximum aneurysm diameter or ulcer depth per the core laboratory

Type	Size Range[a]	Percent Patients (number/total number)
Aneurysm	40 mm – < 50 mm	8.9% (8/90)
	50 mm – < 60 mm	40.0% (36/90)
	60 mm – < 70 mm	36.7% (33/90)
	70 mm – < 80 mm	6.7% (6/90)
	80 mm – < 90 mm	4.4% (4/90)
	90 mm – < 100 mm	3.3% (3/90)
Ulcer	< 20 mm	95.0% (19/20)
	20 mm – < 30 mm	5.0% (1/20)
	30 mm – < 40 mm	0
	40 mm – < 50 mm	0
	50 mm – < 60 mm	0
	60 mm – < 70 mm	0
	70 mm – < 80 mm	0

[a]Diameter for aneurysms and depth for ulcers.

Table 6.1-10 provides the distribution in location of the aneurysm/ulcer.

Table 6.1-10. Location of the primary aneurysm/ulcer as determined by the core laboratory

Location	Percent Patients (number/total number)		
	Aneurysm Patients	Ulcer Patients	All Patients
Location in the thoracic aorta			
Proximal	26.7% (24/90)	50.0% (10/20)	30.9% (34/110)
Middle	53.3% (48/90)	30.0% (6/20)	49.1% (54/110)
Distal	20.0% (18/90)	20.0% (4/20)	20.0% (22/110)

Procedural Information

The majority (71.8%) of procedures were performed under general anesthesia, followed by local anesthesia in 21.8% of procedures. Vascular access was gained via femoral artery cutdown in 62.7% of patients, percutaneously in 36.4% of patients and by using a conduit 0.9% of patients. The mean procedure time was 99.4 ± 53.6 minutes (range 31-362) and the mean procedural blood loss was 121.8 ± 137.7 ml. The mean anesthesia time was 162.7 ± 61.4 minutes and the mean fluoroscopy time was 20.0 ± 20.1 minutes.

Adjunctive procedures for spinal cord protection to prevent paraplegia were performed in 40.0% of patients (72.7% of the adjunctive procedures were cerebral spinal fluid (CSF) drainage), and induced hypotension to ease deployment was performed in 7.3% of patients. The left subclavian artery (LSA) was covered completely in 13% of patients. No LCCA to LSA bypass or LSA transposition were performed.

The access method used to insert the Zenith Alpha™ Thoracic Endovascular Graft is presented in Table 6.1-11. Three types of methods were used: percutaneous (direct needle puncture of the access vessel), cutdown (surgical exposure of the access vessel), and conduit (surgical technique used to bypass prohibitive access vessels). For the percutaneous access method, the procedure time was 88.8 ± 44.7 minutes, blood loss was 128.5 ± 136.4 cc, and incidence of access site complications was 7.3%. For the cutdown/conduit access method, the procedure time was 105.4 ± 57.6 minutes, blood loss was 118.0 ± 139.3 cc, and incidence of access site complications was 5.7%. These data support the use of either method of access for the device.

Table 6.1-11. Access method used to insert the endovascular graft

Type	Percent Patients (number/total number)		
	Aneurysm Patients	**Ulcer Patients**	**All Patients**
Percutaneous	31.1% (28/90)	60.0% (12/20)	36.4% (40/110)
Cutdown	67.8% (61/90)	40.0% (8/20)	62.7% (69/110)
Conduit	1.1% (1/90)	0	0.9% (1/110)

The location of the graft components relative to an identified site is provided as percent of patients in Table 6.1-12.

Table 6.1-12. Graft location per core laboratory

Location	Percent Patients (number/total number)		
	Aneurysm Patients	Ulcer Patients	All Patients
Proximal aspect of graft			
Above LCCA	0	0	0
Below LCCA, above LSA	9.1% (8/88)	30.0% (6/20)	13.0% (14/108)
Below LSA	83.0% (73/88)	60.0% (12/20)	78.7% (85/108)
Unable to assess[a]	8.0% (7/88)	10.0% (2/20)	8.3% (9/108)
Distal aspect of graft			
Above celiac artery	95.5% (84/88)	90.0% (18/20)	94.4% (102/108)
Below celiac artery	0	0	0
Unable to assess[a]	4.5% (4/88)	10.0% (2/20)	5.6% (6/108)

LCCA = left common carotid artery; LSA = left subclavian artery.
[a]All patients had post-procedure angiography but not all imaging was adequate for core laboratory review.

Two patients required axillary-axillary bypasses prior to the index procedure (both from a Japanese site). Additional procedures performed after graft deployment included use of a vessel closure device in 26 patients, LCCA stent placement in 1 patient, LSA stent in 1 patient, LSA coil embolization in 5 patients, femoral endarterectomy in 2 patients, thrombo-endarterectomy and patch right femoral in1 patient, iliac artery stents in 3 patients, and chimney stent to maintain blood flow to the LCCA and LSA coil embolization in one patient. Table 6.1-13 reports additional procedures performed either before or after graft implantation.

Table 6.1-13. Additional procedures

Procedure	Percent Patients (number/total number)	
	Before Graft Deployment	After Graft Deployment
Left carotid artery stent	0	0.9% (1/110)
Left subclavian artery stent	0	0.9% (1/110)
Iliac artery angioplasty	0.9% (1/110)	0
Iliac artery stent	0	2.7% (3/110)
Vessel closure device	0	23.6% (26/110)
Other	1.8% (2/110)[a]	8.2% (9/110)[b]

[a]Two patients from Japan (1040051 and 1040069) underwent axillary-axillary bypass prior to the index procedure.
[b]Two patients (1030005 and 1030044) underwent right femoral endarterectomy after the index procedure. One patient (0465997) underwent thromboendarterectomy and patch right femoral after the index procedure. Five patients (1040023, 1040033, 1040039, 1040051, and 1040069) underwent coil embolization of the left subclavian artery after the index procedure. One patient (1040080) had a chimney stent placed to maintain blood flow to the left common carotid artery and coil embolization of the left subclavian artery after the index procedure.

The device was successfully implanted in 98.2% of patients (2 patients did not receive the device due to the inability to insert/advance the introduction system) and all patients

(100%) survived the endovascular procedure. Overall, the procedural results were as expected for the treatment of patients with aneurysms or ulcers of the descending thoracic aorta.

Clinical Utility Measures

The clinical utility results are presented in Table 6.1-14.

Table 6.1-14. Clinical utility measures

Clinical Utility Measure	Mean ± SD (n, range)[a]		
	Aneurysm	Ulcer	All patients
Duration of ICU stay (days)	2.6 ± 9.9 (n=88, 0 – 91)	0.8 ± 0.6 (n=20, 0 – 2)	2.3 ± 8.9 (n=108, 0 – 91)
Days to resumption of oral fluid intake	0.4 ± 0.6 (n=89, 0 – 3)	0.5 ± 0.8 (n=20, 0 – 3)	0.4 ± 0.6 (n=109, 0 – 3)
Days to resumption of regular diet	1.3 ± 1.1 (n=89, 0 – 6)	1.5 ± 3.1 (n=19, 0 – 14)	1.3 ± 1.6 (n=108, 0 – 14)
Days to resumption of bowel function	2.3 ± 1.5 (n=70, 0 – 8)	2.0 ± 2.1 (n=15, 0 – 8)	2.3 ± 1.6 (n=85, 0 – 8)
Days to ambulation	1.6 ± 1.3 (n=88, 0 – 9)	1.8 ± 2.2 (n=20, 0 – 10)	1.6 ± 1.5 (n=108, 0 – 10)
Days to hospital discharge	7.4 ± 19.6 (n=90, 1 – 185)	5.0 ± 5.3 (n=20, 1 – 19)	7.0 ± 17.8 (n=110, 1 – 185)

[a]Not all clinical utility measures were assessed for all 110 patients.

Devices Implanted

Table 6.1-15 shows the percent of patients who received each type of Zenith Alpha™ Thoracic Endovascular Graft component (proximal, distal, or distal extension) during the initial implant procedure. Also included is the graft diameter range implanted for each component type.

Table 6.1-15. Stent-graft component type deployed

Type	Percent Patients (number/total number)[a]			Graft Diameter Range (All Patients)
	Aneurysm Patients	Ulcer Patients	All patients	
Proximal component (nontapered or tapered)	100% (88/88)	100% (20/20)	100% (108/108)	28 to 46 mm
Distal component	37.5% (33/88)	0	30.6% (33/108)	32 to 46 mm

Ancillary component	27.3% (24/88)[b]	5.0% (1/20)	23.1% (25/108)	28 to 46 mm
Additional proximal component	13.6% (12/88)	5.0% (1/20)	12.0% (13/108)	
Distal extension	14.8% (13/88)[c]	0	12.0% (13/108)	

[a]Two aneurysm patients did not receive a device as the introduction system could not be successfully advanced; therefore, the denominator is 108, not 110.
[b]One patient received both an additional proximal component and a distal extension.
[c]Includes 12 patients who received 1 distal extension, and 1 patient who received 2 distal extensions.

Table 6.1-16 further summarizes the total number of components placed during the initial implant procedure.

Table 6.1-16. Total number of components placed during the initial implant procedure

Main Body Design	Percent Patients (number/total number)[a]		Percent Patients (number/total number)		
			1	2	3
One-piece (proximal only)	Aneurysm Patients	62.5% (55/88)	69.1% (38/55)	29.1% (16/55)	1.8% (1/55)
	Ulcer Patients	100% (20/20)	95.0% (19/20)	5.0% (1/20)	0
	All Patients	69.4% (75/108)	76.0% (57/75)	22.7% (17/75)	1.3% (1/75)
Two-piece (proximal and distal)	Aneurysm Patients	37.5% (33/88)	N/A	78.8% (26/33)	21.2% (7/33)
	Ulcer Patients	N/A	N/A	N/A	N/A
	All Patients	30.6% (33/108)	N/A	78.8% (26/33)	21.2% (7/33)

[a]Two aneurysm patients did not receive a device as the introduction system could not be successfully advanced; therefore, the denominator is 108, not 110.

Table 6.1-17 reports the sizes (diameters and lengths) of the nontapered proximal components used during the initial implant procedure.

Table 6.1-17. Diameters and lengths of nontapered proximal component (ZTLP-P) sizes used

Diameter (mm)	Length (mm)	n
28	132	2
	155	2
30	132	8
	155	2
32	132	7
	155	4
	201	5
34	137	3
	161	6
	209	2
36	137	10
	161	6
	209	1

Diameter (mm)	Length (mm)	n
38	142	7
	167	3
	217	6
40	142	2
	167	3
	217	1
42	121	3
	173	4
44	125	2
	233	1
46	179	4

Table 6.1-18 reports the sizes (diameters and lengths) of the tapered proximal components used during the initial implant procedure.

Table 6.1-18. Diameters and lengths of tapered proximal component (ZTLP-PT) sizes used

Diameter (mm)	Length (mm)	n
34	161	4
	209	1
36	161	7
	209	4
38	167	1
	217	3
42	173	5
44	179	1
46	179	1

Table 6.1-19 reports the sizes (diameters and lengths) of the distal components used during the initial implant procedure.

Table 6.1-19. Diameters and lengths of distal component (ZTLP-D) sizes used

Diameter (mm)	Length (mm)	n
32	160	4
	229	1
34	142	2
	190	1
36	142	3
	190	1
38	147	4
	197	5
40	147	1
42	152	6
44	157	3
46	157	2

Table 6.1-20 reports the size (diameters and lengths) of the ancillary components used during the initial implant procedure.

Table 6.1-20. Diameters and lengths of ancillary component sizes used

Diameter (mm)	Length (mm)	n
28	108	1
32	108	2
34	112	2
36	112	1
38	91	4
42	94	3
46	97	1

Safety Results

The analysis of safety was based on the 110 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of aneurysms/ulcers of the descending thoracic aorta. Table 6.1-21 presents the results of hypothesis testing for the primary safety endpoint (30-day freedom from MAEs). MAEs were defined as the following: all-cause death; Q-wave myocardial infarction; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

Table 6.1-21. Results from primary safety hypothesis testing (MAE endpoint)

Performance Goal	30-day Freedom from MAE Rate	*P*-value	95% Confidence Interval	Performance Goal Met
80.6%	96.4% (106/110)	< 0.001	(91%, 99%)	Yes

The 30-day freedom from MAE rate was 96.4% for the present study, which met the performance goal of 80.6% ($p < 0.001$). Four patients experienced MAEs: 1 patient had a stroke (1040045), 2 patients required ventilation > 72 hours/reintubation (1030062, 1030041), and 1 patient had a stroke and required ventilation > 72 hours/reintubation (1040069).

Death, Rupture, Conversion and MAE

Table 6.1-22 provides the results from Kaplan-Meier analysis for freedom from death (all-cause and TAA-related), rupture, conversion and MAEs through 2 years. Aneurysm-related mortality was defined as death occurring within 30 days of the initial implant procedure or a secondary intervention, or any death adjudicated to be aneurysm-related by the CEC. There has been one TAA-related death (1040069) that occurred at 253 days post-procedure due to aspiration pneumonia, which the CEC had indicated was likely related to the severely debilitating stroke that the patient had suffered on the same day as the procedure. There has been one conversion to open surgical repair (1040073), which occurred at 330 days post-procedure due to aortoesophageal fistula.

Table 6.1-22. Kaplan-Meier estimates freedom from death (all-cause and TAA-related), rupture, conversion, and MAEs

Event	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
All-cause mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	2	1	3	4	1	5	11	1	12
	Cumulative censored[c]	1	0	1	2	0	2	6	1	7	10	1	11
	KM estimate[d]	1.000	1.000	1.000	0.977	0.950	0.972	0.954	0.950	0.953	0.869	0.950	0.884
	Standard error	0.000	0.000	0.000	0.016	0.049	0.016	0.023	0.049	0.020	0.037	0.049	0.032
TAA-related mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[e]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
Rupture	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	0	0	0	0	0	0
	Cumulative censored[c]	1	0	1	4	1	5	10	2	12	21	2	23
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Conversion	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[f]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
MAE[g]	Number at risk[a]	85	20	105	81	19	100	74	18	92	60	18	78
	Cumulative events[b]	4	0	4	7	1	8	12	1	13	24	1	25
	Cumulative censored[c]	1	0	1	2	0	2	4	1	5	6	1	7
	KM estimate[d]	0.956	1.000	0.964	0.922	0.950	0.927	0.864	0.950	0.879	0.722	0.950	0.763
	Standard error	0.022	0.000	0.018	0.029	0.049	0.025	0.037	0.049	0.032	0.049	0.049	0.042

[a]Number of patients at risk at the beginning of the interval.
[b]Total events up to and including the specific interval represents all patients who have had the event. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events in each category.
[c]Total censored patients up to and including the specific interval represents all patients who have met a study exit criteria or for whom data are not available at the specific interval.
[d]At end of interval.
[e]Death due to aspiration pneumonia (1040069).
[f]Conversion due to aortoesophageal fistula, adjudicated by the CEC as procedure-related (1040073).

[g]MAEs were defined as the following: all-cause death; Q-wave myocardial infarction; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

All Adverse Events

Table 6.1-23 presents the Kaplan-Meier estimates for freedom from adverse events according to organ system category.

Table 6.1-23. Kaplan-Meier estimates (freedom from morbidity, by category)

Category	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Access site/incision[a]	Number at risk[i]	84	19	103	78	18	96	72	17	89	62	17	79
	Cumulative events[j]	5	1	6	8	1	9	8	1	9	8	1	9
	Cumulative censored[k]	1	0	1	4	1	5	10	2	12	20	2	22
	KM estimate[l]	0.944	0.950	0.945	0.910	0.950	0.917	0.910	0.950	0.917	0.910	0.950	0.917
	Standard error	0.024	0.049	0.022	0.030	0.049	0.026	0.030	0.049	0.026	0.030	0.049	0.026
Cardiovascular[b]	Number at risk[i]	84	20	104	82	19	101	74	18	92	63	18	81
	Cumulative events[j]	5	0	5	5	0	5	7	0	7	8	0	8
	Cumulative censored[k]	1	0	1	3	1	4	9	2	11	19	2	21
	KM estimate[l]	0.944	1.000	0.955	0.944	1.000	0.955	0.921	1.000	0.935	0.907	1.000	0.924
	Standard error	0.024	0.000	0.020	0.024	0.000	0.020	0.029	0.000	0.024	0.032	0.000	0.026

Category	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Cerebrovascular/ neurological[c]	Number at risk[i]	86	20	106	83	19	102	76	18	94	66	18	84
	Cumulative events[j]	3	0	3	4	0	4	6	0	6	6	0	6
	Cumulative censored[k]	1	0	1	3	1	4	8	2	10	18	2	20
	KM estimate[l]	0.967	1.000	0.973	0.955	1.000	0.963	0.931	1.000	0.943	0.931	1.000	0.943
	Standard error	0.019	0.000	0.016	0.022	0.000	0.018	0.027	0.000	0.022	0.027	0.000	0.022
Gastrointestinal[d]	Number at risk[i]	88	19	107	81	18	99	76	17	93	66	17	83
	Cumulative events[j]	1	1	2	5	2	7	6	2	8	8	2	10
	Cumulative censored[k]	1	0	1	4	0	4	8	1	9	16	1	17
	KM estimate[l]	0.989	0.950	0.982	0.943	0.900	0.935	0.931	0.900	0.926	0.906	0.900	0.905
	Standard error	0.011	0.049	0.013	0.025	0.067	0.024	0.027	0.067	0.025	0.032	0.067	0.029
Pulmonary[e]	Number at risk[i]	85	20	105	81	19	100	74	18	92	66	18	84
	Cumulative events[j]	4	0	4	5	0	5	6	0	6	8	0	8
	Cumulative censored[k]	1	0	1	4	1	5	10	2	12	16	2	18
	KM estimate[l]	0.955	1.000	0.964	0.944	1.000	0.954	0.931	1.000	0.944	0.905	1.000	0.923
	Standard error	0.022	0.000	0.018	0.024	0.000	0.020	0.027	0.000	0.022	0.032	0.000	0.026
Renal[f]	Number at risk[i]	86	20	106	79	19	98	73	18	91	64	18	82
	Cumulative events[j]	3	0	3	7	0	7	10	0	10	12	0	12
	Cumulative censored[k]	1	0	1	4	1	5	7	2	9	14	2	16
	KM estimate[l]	0.967	1.000	0.973	0.921	1.000	0.935	0.885	1.000	0.905	0.859	1.000	0.855
	Standard error	0.019	0.000	0.16	0.029	0.000	0.024	0.034	0.000	0.029	0.038	0.000	0.031
Vascular[g]	Number at risk[i]	85	20	105	80	18	98	71	17	88	55	16	71
	Cumulative events[j]	4	0	4	6	1	7	10	1	11	18	2	20
	Cumulative censored[k]	1	0	1	4	1	5	9	2	11	17	2	19
	KM estimate[l]	0.955	1.000	0.963	0.933	0.950	0.936	0.884	0.950	0.896	0.789	0.894	0.801
	Standard error	0.022	0.000	0.018	0.027	0.049	0.024	0.035	0.049	0.030	0.046	0.071	0.040
Miscellaneous/ other[h]	Number at risk[i]	59	13	72	43	10	53	33	9	42	26	9	35
	Cumulative events[j]	28	7	35	44	10	54	54	10	64	61	10	71
	Cumulative censored[k]	1	0	1	1	0	1	1	1	2	1	1	2
	KM estimate[l]	0.681	0.650	0.675	0.497	0.500	0.497	0.381	0.500	0.402	0.300	0.500	0.335
	Standard error	0.050	0.107	0.045	0.054	0.122	0.048	0.052	0.122	0.048	0.049	0.112	0.046

[a]Access site/incision events included: hematoma (n=5), hernia (n=1), infection (n=2), lymph fistula (n=0), pseudoaneurysm (n=0), seroma (n=1), and wound complication requiring return to operating room (n=0).

[b]Cardiovascular events included: cardiac arrhythmia (n=4), cardiac arrest (n=0), cardiac ischemia (n=1), congestive heart failure (n=1), myocardial infarction (n=3), and refractory hypertension (n=0).

[c]Cerebrovascular/neurological events included: paralysis (n=0), paraplegia (n=0), paraparesis > 30 days (n=1), spinal cord shock (n=0), transient ischemic attack (n=0), and stroke (n=5).
[d]Gastrointestinal events included: bleeding (n=4), bowel ischemia (n=2), infection (n=4), mesenteric ischemia (n=1), and paralytic ileus > 4 days (n=0).
[e]Pulmonary events included: COPD (n=1), hemothorax (n=0), pleural effusion (n=1), pneumonia (n=6), pneumothorax (n=0), pulmonary edema (n=0), pulmonary embolism (n=1), and pulmonary embolism involving hemodynamic instability or surgery (n=0).
[f]Renal events included: renal failure (n=4), UTI (n=6), serum creatinine rise > 30% above baseline resulting in a persistent value > 2.0 mg/dl (n=2).
[g]Vascular events included: aneurysm (n=11), aortobronchial fistula (n=1), aortoesophageal fistula (n=1), aortoenteric fistula (n=0), coagulopathy (n=1), deep vein thrombosis (n=0), dissection (n=3), embolism (n=2), hematoma (n=1), pseudoaneurysm (n=1), thrombosis (n=1), and vascular injury (n=5).
[h]Miscellaneous/other events included: hypersensitivity/allergic reaction (n=1), multi-organ failure (n=2), sepsis (n=2), and other (n=70).
[i]Number of patients at risk at the beginning of the interval.
[j]Total events up to and including the specific interval represents all patients who have had the event. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events in each category.
[k]Total censored patients up to and including the specific interval represents all patients who have met a study exit criteria or for whom data are not available at the specific interval.
[l]At end of interval.

Effectiveness Results

Table 6.1-24 presents the results of hypothesis testing for the primary effectiveness endpoint (12-month device success) for the Zenith Alpha™ Thoracic Endovascular Graft.

Table 6.1-24. Results from primary effectiveness hypothesis testing (device success endpoint)

Performance Goal	12-month Device Success Rate	*P*-value	95% Confidence Interval	Performance Goal Met
80.7%	92.7% (102/110)[a]	< 0.001	(86.2%, 96.8%)	Yes

[a]The performance goal was originally calculated with a 365-day cutoff for inclusion of events (e.g., secondary interventions) and the results in the present study were analyzed in the same fashion for consistency such that the 12-month device success rate was 95.5% (105/110) with a 95% confidence interval of 89.7%, 98.5%. However, there were 3 additional patients in the present study who had an endoleak detected at the 12-month follow-up and subsequently underwent secondary intervention > 365 days after the index procedure; therefore, a conservative analysis was performed that included these 3 additional patients as failures (as shown in the table).

The 12-month device success rate was 92.7% for the present study (using the conservative analysis shown in Table 6.1-24), which met the performance goal of 80.7% ($p < 0.001$). There were 5 patients who did not meet the effectiveness endpoint of 12-month device success (using the original 365-day cutoff for events), as follows. Two patients (1030014, 1030098) did not receive the device due to an inability to insert/advance the introduction system and were therefore technical failures. In patient 1030014 (87-year-old white female), the introduction system became lodged at the aortic bifurcation in the right common iliac artery despite attempts to increase the diameter of the iliac artery. In patient 1030098 (73-year-old white female), the index procedure was aborted due to difficulty inserting a dilator in the left limb of a previous aneurysm repair; the previous endovascular abdominal aortic aneurysm repair made the patient a poor candidate for a conduit. Three patients (1030017, 1030046, 1040073) experienced aneurysm growth greater than 5 mm at the 12-month follow-up, one of whom (1040073) also underwent conversion to open surgical repair 330 days post-procedure due to an aortoesophageal fistula. There were 3 additional patients who had endoleak detected at 12-month follow-up and subsequently underwent secondary intervention > 365 days after the index procedure (1030047, 1030072, 1030095). Sensitivity to missing data, including a worst-case analysis, was performed, and met the performance goal.

Device Performance

Table 6.1-25 presents changes in aneurysm size, as observed from the 30-day (baseline) measurement to each follow-up exam through 2 years (based on core laboratory evaluation). A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Aneurysm growth was associated with detectable endoleak in six patients, four of whom underwent secondary intervention. There was no detectable endoleak in the remaining five patients with aneurysm growth, two of whom had no change in aneurysm size (≤ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak, two required secondary intervention and one had growth at the last available follow-up; each growth was associated with an inadequate seal zone length (i.e., length < 20 mm) as well as graft undersizing. Each patient who had growth that did not resolve spontaneously or was not associated with a Type II endoleak was initially treated for an aneurysm using only a proximal component, underscoring the importance of adhering to the sizing guidelines in the Instructions for Use (IFU), both in terms of component diameter as well as component type and length, which includes the use of a two-component repair (proximal and distal component) when treating aneurysms.

Table 6.1-25. Change in aneurysm diameter/ulcer depth based on results from core laboratory analysis

Item	Percent Patients (number/total number)								
	Aneurysm			Ulcer			All		
	6-month	12-month	2-years	6-month	12-month	2-years	6-month	12-month	2-years
Increase (> 5 mm)	4.2% (3/72) [a,b,c]	4.2% (3/71) [a,c,d]	14.8% (9/61)[a,d,e-k]	0	0	0	3.3% (3/90)	3.4% (3/88)	12.0% (9/75)
Decrease (> 5 mm)	19.4% (14/72)	31.0% (22/71)	24.6% (15/61)	33.3% (6/18)	52.9% (9/17)	64.3% (9/14)	22.2% (20/90)	35.2% (31/88)	32.0% (24/75)
No change (≤ 5 mm)	76.4% (55/72)	64.8% (46/71)	60.7% (37/61)	66.7% (12/18)	47.1% (8/17)	35.7% (5/14)	74.4% (67/90)	61.4% (54/88)	56.0% (42/75)

Note: the number of patients with adequate imaging to assess for size increase reflects the number of exams in which aneurysm diameter/ulcer depth was able to be assessed at each specified time point, whereas the denominators in this table also take into account the availability of a baseline exam to which to compare.

[a]Patient 1030046 – The patient was treated at the time of the index procedure with a single proximal component. The patient underwent a secondary intervention prior to the 2-year follow-up (Table 6.1-30) to treat the unexplained aneurysm growth (i.e., no detectable endoleaks). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a proximal seal length < 20 mm.

[b]Patient 1040060 – The patient has not required a secondary intervention. Per core laboratory evaluation, no endoleaks have been identified in this patient. Aneurysm size was stable at 12 months (< 5 mm increase).

[c]Patient 1040073 – The patient had a Type IIb endoleak, which was treated prior to the 12-month follow-up (Table 6.1-30).

[d]Patient 1030017 – The patient was treated at the time of the index procedure with a single proximal component. The patient had no evidence of detectable endoleak. The patient underwent a secondary intervention beyond 2 years (placement of a distal component 922 days post-procedure for aneurysm growth). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.
[e]Patient 1040034 – The patient has not had a secondary intervention and core laboratory results indicate no growth at 3 years.
[f]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had distal Type I endoleak (Table 6.1-26) and CEC-confirmed migration (Table 6.1-27). A secondary intervention was performed (ancillary component placement) on post-operative day 727 (Table 6.1-30) and no growth was noted at 3-years. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm.
[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was also noted at the 2-year follow-up (Table 6.1-26). The patient underwent a secondary intervention beyond 2 years (ancillary component placement 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing.
[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. Per core laboratory evaluation, a Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak (Table 6.1-26) has been identified in the patient at 2 years (previous endoleaks identified were Type II). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.
[i]Patient 1040041 – The patient was treated at the time of the index procedure with a single proximal component. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient withdrew from the study 906 days post-procedure.
[j]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had a distal Type I endoleak (Table 6.1-26) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing.
[k]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month and 2-year follow-ups (Table 6.1-26). A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. No secondary interventions have been performed to date. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm.

Endoleaks classified by type, as assessed by the core laboratory at each exam period through 2 years, are reported in Table 6.1-26. In total, there were seven patients found to have a Type I (distal) endoleak and two patients found to have a Type III (nonjunctional) endoleak at one or more time points, two of which (one with Type I and one with Type III) had no evidence of the same endoleak at last available follow-up and without the patients having undergone secondary intervention. Endoleak in the other seven patients (five of which required secondary intervention) was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing, which occurred following aneurysm treatment with only a proximal component in six of the patients, underscoring the

importance of adhering to the sizing guidelines in the IFU, both in terms of component diameter as well as component type and length, including the use of a two-component repair (proximal and distal components) when treating aneurysms.

Table 6.1-26. Endoleak based on results from core laboratory analysis

Type	Percent Patients (number/total number)											
	1-month			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Any (new only)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	4.1% (3/73)	5.6% (1/18)	4.4% (4/91)	4.5% (3/66)	0	3.6% (3/83)	8.5% (5/59)	0	6.8% (5/73)
Any (new and persistent)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	11.0% (8/73)	11.1% (2/18)	11.0% (10/91)	10.6% (7/66)	0	8.4% (7/83)	16.9% (10/59)	0	13.7% (10/73)
Multiple	2.4% (2/82)[a]	0	2.0% (2/102)	2.7% (2/73)[a]	0	2.2% (2/91)	1.5% (1/66)	0	1.2% (1/83)	0	0	0
Proximal Type I	0	0	0	0	0	0	0	0	0	0	0	0
Distal Type I	2.4% (2/82)[a,b]	0	2.0% (2/102)	4.1% (3/73)[a,b,d]	0	3.3% (3/91)	4.5% (3/66)[b,d,e]	0	3.6% (3/83)	8.5% (5/59)[b,e,g-i]	0	6.8% (5/73)
Type II	7.3% (6/82)[a]	0	5.9% (6/102)	9.6% (7/73)[a,b]	5.6% (1/18)	8.8% (8/91)	6.1% (4/66)[b]	0	4.8% (4/83)	6.8% (4/59)	0	5.5% (4/73)
Type III	0	5.0% (1/20)[c]	1.0% (1/102)	0	5.6% (1/18)[c]	1.1% (1/91)	1.5% (1/66)[f]	0	1.2% (1/83)	0	0	0
Type IV	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	1.2% (1/82)	5.0% (1/20)	2.0% (2/102)	0	0	0	0	0	0	1.7% (1/59)	0	1.4% (1/73)

[a]Patient 0463776 – Distal Type I and Type IIb endoleaks were noted at the 1- and 6-month follow-ups. The endoleak type was noted as unknown at last follow-up (unscheduled follow-up at day 300); a decrease in aneurysm size was also noted at last follow-up. No secondary interventions have been performed to date and the patient has since withdrawn from the study.

[b]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month and 2-year follow-ups. A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. The patient also had aneurysm growth (Table 6.1-25). No secondary interventions have been performed to date. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm.

[c]Patient 1040051 – The Type III (nonjunctional) endoleak noted at the 1-month and 6-month follow-ups was no longer present at the 12-month follow-up. The location of the endoleak coincided with an area of prominent calcification in the aorta. No secondary interventions have been performed to date and the patient has not demonstrated an increase in aneurysm size.

[d]Patient 1030072 – A distal Type I endoleak was noted at the 6-month and 12-month follow-ups. A secondary intervention has occurred (for the site-reported reason of distal Type I endoleak after 12-month follow-up). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient underwent a secondary intervention on post-operative day 420 (Table 6.1-30) and there was no endoleak detected at the 2-year follow-up.

[e]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted at the 12-month follow-up (and again at an unscheduled CT (596 days post procedure)) and the 2-year follow-up, at which time the patient underwent secondary intervention. The patient also had aneurysm growth (Table 6.1-25) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention (ancillary component placement) 727 days post-procedure (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. There was no endoleak detected at the 3-year follow-up.

[f]Patient 1030095 – The patient was treated at the time of the index procedure with a single proximal component. A Type III (nonjunctional) endoleak was noted at the 12-month follow-up (a secondary intervention involving distal component placement was performed after the 12-month follow-up for the site-reported reason of distal Type I endoleak; Table 6.1-30). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) in combination with the site-reported reason for secondary intervention (distal Type I, not Type III, endoleak) suggest graft undersizing. Patient has subsequently withdrawn from the study on post-operative day 695.

[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25) and underwent a secondary intervention beyond 2 years (ancillary component placement 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing.

[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. Per core laboratory evaluation, a Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak has been identified in the patient at 2 years (previous endoleaks identified were Type II). The patient also had aneurysm growth (Table 6.1-25). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.

[i]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had aneurysm growth (Table 6.1- 25) and CEC-confirmed migration (Table 6.1-27) and underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing.

The results for migration through 2 years, as confirmed by the CEC, are provided in Table 6.1-27. There were three cases of CEC-confirmed migration (two also with aneurysm growth, distal Type I endoleak, and the need for secondary intervention), each of which was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing and occurred following aneurysm treatment with only a proximal component, underscoring the importance of adhering to the sizing guidelines in the IFU, both in terms of component diameter as well as component type and length, including the use of a two-component repair (proximal and distal components) when treating aneurysms.

Table 6.1-27. Percent of patients (aneurysm and ulcer) with CEC-confirmed migration (date of first occurrence)

Item	Percent Patients (number/total number)		
	6-month	12-month	2-year
Migration (> 10 mm)	0% (0/94)	0% (0/92)	3.9% (3/77)[a,b,c]

[a]Patient 1030012 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. There was no evidence of endoleak, and the aneurysm size has continuously decreased from 61 mm at 1 month to 40 mm at 2 years and 38 mm at 3 years. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.

[b]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had aneurysm growth (Table 6.1-25), distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.

[c]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had aneurysm growth (Table 6.1-25), a distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing

The results from core laboratory analysis for graft kink/compression through 2 years are summarized in Table 6.1-28.

Table 6.1-28. Core laboratory reports of graft kink/compression

Item	30-day	6-month	12-month	2-year
Kink/compression	0	0	0	1.3% (1/77)[a]

[a]Patient 0468761 – The patient had a kink in the proximal and distal components identified by the core laboratory on the 2-year CT scan. There were no clinical sequelae associated with the kink; at the 2-year follow-up, the aneurysm had decreased in size and the device was patent. The patient died prior to the next follow-up visit.

CEC-confirmed device integrity observations at each exam period through 2 years are summarized in Table 6.1-29.

Table 6.1-29. CEC-confirmed loss of device integrity

Finding	Percent Patients (number/total number)											
	30-day			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Barb separation	0	0	0	0	0	0	0	0	0	0	0	0
Stent fracture	1.2% (1/85)[a]	0	1.0% (1/105)	1.3% (1/80)[a]	0	1.0% (1/98)	1.3% (1/75)[a]	0	1.1% (1/92)	1.6% (1/63)[a]	0	1.3% (1/77)
Component separation	0	0	0	0	0	0	0	0	0	0	0	0

[a]Patient 1030069 – Patient had a report of a single stent fracture (of the second covered stent in the proximal device) seen on the 30-day, 6-month, 12-month and 2-year x-rays. Nothing uncharacteristic regarding the anatomy or deployment of the graft was observed. This patient has had no clinical sequelae from the stent fracture.

Tables 6.1-30 and 6.1-31 summarize the site-reported reasons for secondary intervention and types of secondary intervention, respectively.

Table 6.1-30. Site-reported reasons for secondary intervention (all patients)

Reason	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Device migration	0	0	0	1[g]
Endoleak				
Type I proximal	0	0	0	0
Type I distal	0	0	0	3[d,g,h]
Type II	0	0	1[b]	0
Type III (graft overlap joint)	0	0	0	0
Type III (hole/tear in graft)	0	0	0	0
Type IV (through graft body)	0	0	0	1[i]
Unknown	0	0	0	0
Other	1[a]	0	1[c]	2[e,f]

[a]Patient 1040058 (ulcer) – Patient had pre-planned left subclavian artery embolization and right-to-left subclavian artery bypass 7 days after the index procedure.
[b]Patient 1040073 (aneurysm) – Patient had two separate secondary interventions for Type II endoleak: unsuccessful attempt at placing embolization coils in the intercostal artery, followed by successful direct puncture of the aneurysm with delivery of N-butyl cyanoacrylate.
[c]Patient 1040037 (aneurysm) – Patient had additional component placed for aortic dissection proximal to the study device 324 days after the index procedure.
[d]Patient 1030072 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal components and balloon angioplasty 420 days after the index procedure.
[e]Patient 0467042 (aneurysm) – Patient had a dissection distal to the most distal stent. Ancillary components were placed 433 days after the index procedure.
[f]Patient 1030046 (aneurysm) – Patient had observed progression of disease treated with additional proximal and distal components 594 days after the index procedure.
[g]Patient 1030047 (aneurysm) – Patient had observed device migration and Type I distal endoleak treated with ancillary components 727 days after the index procedure.
[h]Patient 1030095 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal components 534 days after the index procedure.
[i]Patient 1040054 (aneurysm) – Patient had persistent Type IV endoleak per site analysis (unknown type endoleak per core laboratory analysis) treated with ancillary components 599 days after the index procedure.

Table 6.1-31. Types of secondary interventions

Type*	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Percutaneous				
Ancillary component placed	0	0	1[b]	6[d-i]
Balloon angioplasty	0	0	0	1[d]
Coil embolization	0	0	0	0
Stent	0	0	0	0
Thrombectomy	0	0	0	0
Thrombolysis	0	0	0	0
Other	0	0	1[b]	0

Type*	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Surgical				
Conversion to open repair	0	0	0	0
Surgical bypass procedure	0	0	0	0
Other	1[a]	0	0	0
Other	0	0	1[c]	0

*A patient may have had more than one treatment type.
[a-i]Refer to the footnotes in Table 6.1-30 for additional details.

Gender Subset Analysis

There was nearly an equal proportion of males (n = 64, 58.2%) and females (n = 46, 41.8%) enrolled in this study, allowing for further analysis of outcomes by gender. There was no significant difference in age between male (70.7 ± 9.9 years; 42 – 85 years) and female (74.3 ± 9.4 years; 44 – 92 years) patients. Furthermore, the access method used (cutdown vs. percutaneous vs. conduit) was not significantly different between male (56.3% cutdown, 43.8% percutaneous, 0% conduit) and female (71.7% cutdown, 26.1% percutaneous, 2.2% conduit) patients.

No significant differences between males and females with respect to primary safety and effectiveness endpoints were found. For the primary safety endpoint, the 30-day freedom from MAE rate was 96.9% (62/64) for males and 95.7% (44/46) for females. For the primary effectiveness endpoint, the 12-month device success rate was 96.9% (62/64) for males and 93.5% (43/46) for females. Overall, males and females treated with the Zenith Alpha™ Thoracic Endovascular Graft had similar outcomes, indicating the device is likely to be equally safe and effective for both males and females.

Summary

All but 2 patients received at least one proximal component, and approximately one-third of patients also received a distal component (i.e., a two-piece system), as compared to approximately two-thirds of patients in the previous study who were treated with a two-piece system. Therefore, a two-component repair was less often used in this study compared to the previous study, despite similar percentages of patients from both studies having been treated for aneurysms. The IFU for the Zenith Alpha™ Thoracic Endovascular Graft was therefore updated to emphasize the importance of a two-component repair when treating aneurysms given that the reports of growth, migration, and distal Type I endoleak tended to occur in only aneurysm patients who were treated using a single proximal component.

Two patients did not receive a device in this study due to an inability to advance/gain access to the target treatment site; 2 patients also did not receive a device in the previous study for similar reasons. In patients where access was gained (n = 108), all devices were deployed successfully in the intended location and all vessels were patent at the time of deployment. An access conduit was necessary for graft delivery in 0.9% of patients, and percutaneous access was used in 36% of patients.

There were no deaths within 30 days of endovascular repair. There was one TAA-related death within 365 days, resulting in a 99% freedom from TAA-related mortality at 1 year. There were no ruptures reported at any follow-up time period. One patient underwent conversion to open repair 330 days post-procedure due to an aortoesophageal fistula; the CEC adjudicated the event as related to the procedure. The patient survived the surgical repair and investigational device explant and has since exited the study. Patients experienced adverse events in each of the organ system categories.

A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Aneurysm growth was associated with detectable endoleak in six patients, four of whom underwent secondary intervention. There was no detectable endoleak in the remaining five patients with aneurysm growth, two of whom had no change in aneurysm size ($\leq$ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak, two required secondary intervention and one had growth at the last available follow-up; each growth was associated with an inadequate seal zone length (i.e., length < 20 mm) as well as graft undersizing.

The majority of endoleaks detected were Type II, and there were no proximal Type I or Type IV endoleaks at 24 months. In total, there were seven patients found to have a Type I (distal) endoleak and two patients found to have a Type III (nonjunctional) endoleak at one or more time points, two of which (one with Type I and one with Type III) had no evidence of the same endoleak at last available follow-up and without the patients having undergone secondary intervention. Endoleak in the other seven patients (five of which required secondary intervention) was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing.

There were three cases of CEC-confirmed migration (two also with aneurysm growth, distal Type I endoleak, and the need for secondary intervention), each of which was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft

undersizing. There was one report of loss of device integrity (a single stent fracture) within 24 months, but with no adverse clinical sequelae.

In total, nine patients required a secondary intervention within 24 months for the site reported reasons of left subclavian artery embolization with bypass (n=1), Type II endoleak (n=1), distal Type I endoleak (n=2), distal Type I endoleak and migration (n=1), Type IV endoleak (n=1), disease progression (n=1), and aortic dissection (n=2).

Both the safety (30-day freedom from MAEs) and effectiveness (12-month device success) hypotheses were met. Overall, the results provide a reasonable assurance of the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft.

6.2. Clinical Study for the BTAI Indication

The Zenith Alpha™ Thoracic Endovascular Graft clinical study is a prospective, nonrandomized, noncomparative, single-arm, multicenter study that was conducted to evaluate the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with BTAI. Enrollment in the clinical trial began on January 23, 2013 and was completed May 7, 2014. Seventeen US institutions enrolled a total of 50 patients in the study for the BTAI indication under IDE G120085. The data presented herein were collected through April 1, 2015.

The Zenith Alpha™ Thoracic Endovascular Graft for BTAI study had two endpoints. The primary safety endpoint was all-cause and aortic-injury-related mortality at 30 days, the latter of which was defined as any death determined by the independent CEC to be causally related to the initial implant procedure, secondary intervention, or rupture of the transected aorta. The primary effectiveness endpoint was device success at 30 days, which was defined as successful access of the injury site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location with patency at the time of deployment completion (technical success) plus none of the following at 30 days: device collapse, Type I or III endoleak requiring reintervention, or conversion to open surgical repair. All data were analyzed using descriptive statistics. Data were not analyzed for the purpose of statistical inference, as BTAI patients typically have extensive concomitant injuries that would confound the interpretation of statistical comparisons to alternative treatments.

An independent core laboratory analyzed all patient imaging. An independent CEC adjudicated relevant adverse events, including all patient deaths. An independent DSMB monitored the clinical trial according to an established safety monitoring plan.

The study follow-up schedule (Table 6.2-1) consisted of imaging (CT) and clinical assessments at post-procedure (clinical assessment only at pre-discharge), 30 days, 6 months, 12 months, and yearly thereafter through 5 years.

Table 6.2-1. Study follow-up schedule

	Pre-op	Intra-op	Post-procedure	30-day	6-month	12-month[c]
Clinical exam	X		X	X	X	X
Blood tests	X		X			
CTA	X[a]			X[b]	X[b]	X[b]
Angiography		X				

[a]The CTA must be obtained as close as possible to the study procedure.

[b]MR or noncontrast CT imaging may be used for those patients experiencing renal failure or who are otherwise unable to undergo contrast-enhanced CT scan, with TEE being an additional option in the event of suboptimal MR imaging.
[c]Performed yearly for 5 years.

Although the primary safety and effectiveness endpoints were evaluated at 30 days, patient data presented herein include longer-term follow-up that was available at the time of the data lock (April 1, 2015). Table 6.2-2 reports the percent of follow-up data available through 24 months.

Table 6.2-2. Follow-up availability

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]			Events Occurring Before Next Interval			
		Clinical	CT[c]	ND	Endoleak	Migration	Aortic Injury Healing	Death	Conversion to Open Repair	Lost to Follow-up/ Withdrawal	Not Due for Next Visit
Operative	50	50/50 (100%)	NA	0	NA	NA	NA	0[d]	0	0	0
30-day	50[d]	46/50 (92.0%)	43/50 (86.0%)	0	42/50 (84.0%)	10/50 (20.0%)[f]	42/50 (84.0%)	5[d]	0	4	0
6-month	41	32/41 (78.0%)	34/41 (82.9%)	0	34/41 (82.9%)	33/41 (80.5%)	34/41 (82.9%)	0	1	1	0
12-month	39	26/39 (66.7%)	26/39 (66.7%)	11	25/39 (64.1%)	20/39 (51.3%)	25/39 (64.1%)	0	0	2	32
24-month	5	0.0% (0/5)	0.0% (0/5)	5	0.0% (0/5)	0.0% (0/5)	0.0% (0/5)	0	0	0	5

ND – Visit not done, but patient still eligible for follow-up.
NA – Not assessed.
[a]Site-submitted data.
[b]Based on core laboratory analysis – Does not include imaging exams received by the core laboratory for analysis, but that have not yet been analyzed.
[c]Includes MRI or TEE imaging (which is allowed per protocol) when a patient is unable to receive contrast medium due to renal failure.
[d]Patient 1200054 – The patient underwent 30-day follow-up (CT scan and clinical exam) 22 days post-procedure before exiting the study due to death 24 days post-procedure.
[e]As the 30-day time point represented the baseline CT for migration assessments, the core laboratory only assessed 30-day migration for 10 patients, who had an unscheduled post-procedure CT scan that was used as the baseline scan.

Demographics and Patient Characteristics

The demographics and patient characteristics are presented in Table 6.2-3. Height and weight measurements were not assessed.

Table 6.2-3. Demographics and patient characteristics

Demographic	Mean ± SD (n, range) or Percent Patients (number/total number)
Age (years)	
All patients	42.7 ± 18.7 (n=50, 18 – 89)
Male	42.3 ± 19.6 (n=44, 18 – 89)
Female	45.5 ± 11.0 (n=6, 28 – 59)
Gender	
Male	88.0% (44/50)
Female	12.0% (6/50)
Ethnicity	
White	76.0% (38/50)
Hispanic or Latino	10.0% (5/50)
Black or African American	8.0% (4/50)
American Indian or Alaska Native	0
Asian	6.0% (3/50)
First Nations	0

The medical history and comorbid medical conditions for the patient cohort are presented in Table 6.2-4.

Table 6.2-4. Pre-existing comorbid medical conditions

Medical History	Percent Patients (number/total number)[a]
Cardiovascular	
Cardiac arrhythmia	2.0% (1/50)
Congestive heart failure (CHF)	0
Coronary artery disease	6.0% (3/50)
Myocardial infarction (MI)	4.0% (2/50)
Surgical or percutaneous treatment	6.0% (3/50)
Vascular	
Thromboembolic event	0
Peripheral vascular disease	0
Aneurysm (patient history)	0
Dissection	0
Bleeding diathesis or uncorrectable coagulopathy	0
Carotid endarterectomy	0
Hypertension	26.0% (13/50)
Pulmonary	
Chronic obstructive pulmonary disease (COPD)	2.0% (1/50)
Renal	
Chronic renal insufficiency	0
Dialysis	0
Endocrine	
Diabetes	10.0% (5/50)

Medical History	Percent Patients (number/total number)[a]
Infectious disease	
Sepsis	0
Hepatobiliary	
Liver disease	4.0% (2/50)
Neoplasms	
Cancer	6.0% (3/50)
Neurologic	
Paralysis	0
Paraparesis	0
Stroke	0
Transient ischemic attack/reversible ischemic neurologic deficit	0
Connective tissue	
Marfan Syndrome	0
Ehlers Danlos	0
Substance use	
Past or current smoker	46.0% (23/50)

Assessments of pre-procedure risk (ASA classification, Glasgow coma scale, and injury severity score) are presented in Table 6.2-5.

Table 6.2-5. Pre-procedure risk

Measure	Percent Patients (number/total number) or Mean ± SD or Median (n, range)
ASA classification	
1	0
2	8.0% (4/50)
3	26.0% (13/50)
4	50.0% (25/50)
5	16.0% (8/50)
Glasgow coma scale (GCS)	
Mild ≥ 13	48.0% (24/50)
Moderate 9 – 12	18.0% (9/50)
Severe ≤ 8	34.0% (17/50)
Injury severity score (ISS)	
Mean	31.0 ± 14.0 (n=50, 3 – 66)
Median	29.0 (n=50, 3 – 66)

Concomitant injuries are presented in Table 6.2-6.

Table 6.2-6. Concomitant injuries

Injury	Percent Patients (number/total number)
Abdominal injuries (solid organ, bowel, bladder)	62.0% (31/50)
Head injury	40.0% (20/50)
Long bone fracture	58.0% (29/50)
Lung injury	60.0% (30/50)
Neurological deficits	18.0% (9/50)

Injury	Percent Patients (number/total number)
Pelvis fracture	30.0% (15/50)
Rib fractures	72.0% (36/50)
Scapula fracture	12.0% (6/50)
Unstable fractures (cervical/thoracic/lumbar spine)	14.0% (7/50)
Other[a]	34.0% (17/50)

[a]Other concomitant injuries as reported by the sites include: open fracture right tibia and fibula, left knee traumatic arthrotomy, right radial and ulnar fractures, C6-C7 abnormality (widening of space), grade 11B left ICA dissection at C2 level, open dislocation of ankle, closed fracture of distal phalanx or phalanges (thumb), open scalp wound, open pubis fracture, closed fracture of the nasal bones, closed fracture of pubis, closed fracture of shaft of the tibia, fracture of navicular (scaphoid) bone of foot, respiratory distress syndrome, pneumonia, clavicle fracture, right external ventricular drain placement, small hemorrhagic left pleural effusion, small left pneumothorax, right first metatarsal fracture, right orbital floor fracture, right maxillary sinus fractures, facial fractures, severed left lower extremity, bruising on the abdomen, left hip contusion, right and left knee abrasions, history of seizure disorder, and bilateral nasal bone fracture.

The etiology of thoracic aortic injury for the patients enrolled in the study is presented in Table 6.2-7.

Table 6.2-7. Etiology of the thoracic injury

Etiology of Thoracic Injury	Percent Patients (number/total number)
Fall	4.0% (2/50)
Motor vehicle accident	72.0% (36/50)
Motorcycle accident	14.0% (7/50)
Pedestrian hit by a motor vehicle	6.0% (3/50)
Other[a]	4.0% (2/50)[a]

[a]One patient (1200070) was riding a moped and was hit by a motor vehicle. One patient (1200046) was riding a bicycle and was hit by a motor vehicle.

The results from core laboratory analysis of pre-procedure aortic injury grade are provided in Table 6.2-8.

Table 6.2-8. Pre-procedure aortic injury grade based on core laboratory analysis

Characteristic	Percent Patients (number/total number)
Traumatic aortic injury grade	
1 (intimal tear)	0
2 (intramural hematoma/large intimal flap)	8.0% (4/50)
3 (pseudoaneurysm)	86.0% (43/50)
4 (rupture)	6.0% (3/50)

Table 6.2-9 reports presenting anatomical dimensions.

Table 6.2-9. Presenting anatomical dimensions reported per the core laboratory

Measure	Mean ± SD (n, range)
Aortic injury Maximum diameter (mm) Length (mm)	 31.5 ± 6.4 (n=47, 21.3 – 48.4) 31.5 ± 18.0 (n=49, 9.8 – 118.6)
Length from left common carotid artery to most proximal extent of aortic injury (mm)	27.8 ± 13.3 (n=48, 0.1 – 73.1)
Length from celiac artery to most distal extent of aortic injury	186.0 ± 28.8 (n=41, 103.9 – 252.7)
Maximum aortic diameter in intended proximal seal zone (mm)	27.9 ± 6.0 (n=45, 19.7 – 48.2)
Maximum aortic diameter in intended distal seal zone (mm)	25.2 ± 5.9 (n=38, 16.8 – 41.3)
Right common iliac artery Narrowest segment (mm)	 6.7 ± 1.6 (n=38, 3.5 – 10.3)
Left common iliac artery Narrowest segment (mm)	 6.9 ± 1.5 (n=38, 3.9 – 9.7)

Procedural Information

The majority (98.0%) of procedures were performed under general anesthesia. Vascular access was gained via femoral artery cutdown in 56.0% of patients and percutaneously in 44.0% of patients. Adjunctive procedures to prevent paraplegia, specifically CSF drainage, were performed in 4.0% of patients, and induced hypotension for accurate deployment was used in 10.0% of patients. The LSA was covered partially or completely in 47.8% of patients. No supra-aortic vessel bypass was performed. The most common location of the aortic injury was at the isthmus in 56.0% of patients, followed by the distal descending thoracic aorta in 34.0% of patients. The mean procedure time was 85.3 ± 44.3 minutes (range 34-278 minutes) and the mean procedural blood loss was 102.5 ± 144.6 ml. The mean anesthesia time was 182.9 minutes and the mean fluoroscopy time was 8.6 ± 8.3 minutes. The access techniques used are presented in Table 6.2-10.

Table 6.2-10. Access technique used to insert the endovascular graft

Type	Percent Patients (number/total number)
Percutaneous	44.0% (22/50)[a]
Cutdown	56.0% (28/50)
Conduit	0

[a]For 2 patients, device delivery was preformed percutaneously; however, subsequent cutdown was required to close the access site due to a percutaneous closure device failure (1200075) and to treat femoral artery stenosis (1200042).

The location of the graft components relative to an identified site is provided in Table 6.2-11.

Table 6.2-11. Graft location based on core laboratory analysis

Location	Percent Patients (number/total number)
Proximal edge of graft material	
Above left common carotid artery	0
Below left common carotid artery, above left subclavian artery	47.8% (22/46)*
Below left subclavian artery	52.1% (24/46)
Distal aspect of graft	
Above celiac artery	100% (46/46)
Below celiac artery	0

*The left subclavian artery was completely covered in 7 patients and partially covered in 15 patients.

All patients survived the endovascular procedure. Technical success was achieved in all patients (100%). Overall, the procedural results were as expected for the treatment of patients with BTAI.

Clinical Utility Measures

The clinical utility results are presented in Table 6.2-12.

Table 6.2-12. Clinical utility measures

Clinical Utility	Mean ± SD (n, range)
Duration of ICU stay (days)	17.8 ± 20.1 (n=50, 1 – 126)[a]
Duration of mechanical ventilation (days)	13.4 ± 20.9 (n=50, 0 – 127)[a]
Days to resumption of oral fluid intake	10.4 ± 14.9 (n=45, 0 – 78)[b-d]
Days to resumption of regular diet	14.3 ± 18.8 (n=44, 0 – 99)[a-d]
Days to resumption of bowel function	5.8 ± 4.9 (n=46, 0 – 24)[e]
Days to hospital discharge	25.0 ± 24.3 (n=50, 2 – 125)[a]

[a]Patient 1200079 required ICU stabilization 1 day prior to the procedure (126 days total) and required mechanical ventilation for 2 days prior to the procedure (127 days total). The BTAI treatment was postposed as the patient required further resuscitation and stabilization of a left lower extremity injury. This patient has not resumed regular diet intake and is currently receiving nutrition from a percutaneous endoscopic gastrostomy (PEG) tube.
[b]Days to resumption of oral fluid intake and regular diet were not reported for patient 1200041. The patient was placed on a feeding tube until death occurred on post-operative day 36.
[c]Three patients (1200024, 1200051, and 1200057) were discharged from the hospital before resumption of oral fluid intake and regular diet occurred.
[d]Days to resumption of oral fluid intake and regular diet were unknown for 1 patient (1200074).
[e]Days to resumption of bowel function was unknown for 4 patients (1200015, 1200023, 1200041, and 1200067).

Devices Implanted

Table 6.2-13 presents the percent of patients who received one or more Zenith Alpha™ Thoracic Endovascular Graft proximal components during the implant procedure. Also reported is the range of graft diameters that were implanted. One patient (1200012) received two study components (the second component was placed to extend graft coverage distally). While all other patients received a single study component, it should be noted that one patient (1200040) received two commercial components in combination with a single study component. The first study component and first commercial component placed were the same diameter and had been undersized as measurements were taken from a pre-procedure CT scan performed while the patient was not fully resuscitated; the final component placed (second commercial component) was larger in diameter than the two previously placed components. The IFU therefore underscores that graft sizing for BTAI should be based on measurements in a fully resuscitated patient.

Table 6.2-13. Number of study components deployed and graft diameter range

Number of Components Deployed	Percent Patients (number/total number)	Graft Diameter Range
1	98.0% (49/50)[a]	18 to 38 mm
2	2.0% (1/50)[b]	

[a]Patient 1200040 received one study component and two commercial components. The first study component and first commercial component placed were the same diameter and had been undersized, as measurements were taken from a pre-procedure CT scan performed while the patient was not fully resuscitated; the final component placed (second commercial component) was larger in diameter than the two previously placed components.
[b]Patient 1200012 received two study components; the additional study component was placed to extend graft coverage distally.

Table 6.2-14 reports the specific sizes (diameters and lengths) of the nontapered proximal components used during the initial implant procedure.

Table 6.2-14. Diameters and lengths of nontapered proximal component (ZTLP-P) sizes used

Diameter (mm)	Length (mm)	n
18	105	2
20	105	1
22	105	1
24	105	11
26	105	6
28	109	4
30	109	6
32	109	3[a]
34	113	3
36	113	1

Diameter (mm)	Length (mm)	n
38	117	3

[a]Patient 1200012 received two 32 x 109 mm proximal components.

Table 6.2-15 reports the specific sizes (diameters and lengths) of the tapered proximal components used during the initial implant procedure.

Table 6.2-15. Diameters and lengths of tapered proximal component (ZTLP-PT) sizes used

Diameter (mm)	Length (mm)	n
26	105	9
30	108	1

The access technique used is presented in Table 6.2-16.

Table 6.2-16. Access technique used to insert the endovascular graft

Type	Percent Patients (number/total number)
Percutaneous	44.0% (22/50)[a]
Cutdown	56.0% (28/50)
Conduit	0

[a]For 2 patients, device delivery was preformed percutaneously; however, subsequent cutdown was required to close the access site due to a percutaneous closure device failure (1200075) and to treat femoral artery stenosis (1200042).

Safety Results

The analysis of safety was based on the 50 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of BTAI. The primary safety endpoint for the study was all-cause and aortic-injury-related mortality at 30 days. Aortic-injury-related mortality was defined as any death determined by the independent CEC to be causally related to the initial implant procedure, secondary intervention, or rupture of the transected aorta. Table 6.2-17 presents the primary safety endpoint results from the study of the Zenith Alpha™ Thoracic Endovascular Graft for BTAI.

Table 6.2-17. Results for the primary safety endpoint (30-day mortality)

Endpoint	Measure	Percent Patients (number/total number)
Safety	30-day all-cause mortality	2.0% (1/50)
	30-day aortic-injury-related mortality	0.0% (0/50)

There were no aortic-injury-related deaths within 30 days of the index procedure. The only death (1200054) was adjudicated as unrelated to BTAI repair by the CEC (death due to respiratory failure), resulting in an all-cause mortality rate of 2.0%.

Four deaths were reported beyond 30 days (1 related to BTAI repair; 3 unrelated to BTAI repair). The one death adjudicated as related to BTAI repair occurred on day 116 due to exsanguination from aortoesophageal fistula (1200024). This same patient previously underwent reintervention on day 74 to treat a pseudoaneurysm proximal to the originally placed stent-graft (see Table 6.2-23), which may have resulted from an infectious process.

Adverse Events

Table 6.2-18 reports the frequency of patients with adverse events in each organ system within 0 to 30 days, 31 to 365 days, or 366 to 730 days following BTAI repair.

Table 6.2-18. Number of patients experiencing adverse events by category

Category	0-30 Days	31-365 Days	366-730 Days
Access site/incision[a]	4	0	0
Cardiovascular[b]	7	1	0
Cerebrovascular/neurological[c]	2	0	0
Gastrointestinal[d]	5	1	0
Pulmonary[e]	20	2	1
Renal/urologic[f]	5	4	0
Vascular[g]	7	5	0
Miscellaneous[h]	22	19	2

Note: The same patient may have experienced events in multiple categories.
[a]Access site/incision events included: hematoma (n=2), infection (n=0), dehiscence (n=0), seroma (n=0), pseudoaneurysm (n=1), hernia (n=0), and wound complication requiring return to the operating room (n=1).
[b]Cardiovascular events included: cardiac arrhythmia requiring intervention (n=7), cardiac arrest (n=1), congestive heart failure (n=0), myocardial infarction (n=0), and refractory hypertension (n=0).
[c]Cerebrovascular/neurological events included: paraplegia (n=0), paraparesis > 30 days (n=0), spinal cord shock (n=0), transient ischemic attack (n=0), and stroke (n=2).
[d]Gastrointestinal events included: bowel obstruction (n=2), infection (n=1), paralytic ileus > 4 days (n=1), mesenteric ischemia (n=0), and bleeding (n=2).
[e]Pulmonary events included: respiratory distress syndrome (n=3), COPD (n=0), pneumonia (n=16), hemothorax (n=2), pneumothorax (n=2), pulmonary edema (n=1), pleural effusion requiring intervention (n=3), and pulmonary embolism (n=2).
[f]Renal/urologic events included: renal failure (n=1), UTI requiring antibiotics (n=7), and serum creatinine rise > 30% above baseline resulting in a persistent value > 2 mg/dl (n=1).
[g]Vascular events included: aortic aneurysm (n=0), aortoesophageal fistula (n=1), aortobronchial fistula (n=0), aortoenteric fistula (n=0), hematoma (n=1), arterial thrombosis (n=1), pseudoaneurysm requiring intervention (n=2), coagulopathy (n=0), deep vein thrombosis (n=6), aortic dissection (n=1), aortic rupture (n=0), and distal embolization with tissue loss (n=0).
[h]Miscellaneous events included: device infection (n=0), hypersensitivity/allergic reaction (n=0), multi-organ failure (n=3), sepsis (n=2), and other (n=30).

There were no ruptures or conversions to open repair within 30 days.

Effectiveness Results

The analysis of effectiveness was based on the 50 patients enrolled in the Zenith Alpha™ Thoracic Endovascular Graft pivotal study for the treatment of BTAI. The primary effectiveness endpoint was device success at 30 days. Device success at 30 days was defined as successful access of the injury site and deployment of the Zenith Alpha™ Thoracic Endovascular Graft in the intended location with patency at the time of deployment completion (technical success), plus none of the following at 30 days: device collapse, Type I or Type III endoleak requiring reintervention, or conversion to open surgical repair. Table 6.2-19 presents the primary effectiveness endpoint results from the study of the Zenith Alpha™ Thoracic Endovascular Graft for BTAI.

Table 6.2-19. Results for the primary effectiveness endpoint (30-day device success)

Endpoint	Measure	Percent Patients (number/total number)
Effectiveness	30-day device success	96.0% (48/50)

Device success was achieved in 96.0% of patients. There were 2 patients (1200012, 1200033) who did not meet the effectiveness endpoint of 30-day device success for the following reasons: 1 patient (1200012) had device compression and 1 patient (1200033) had a site-reported Type I endoleak requiring secondary intervention – note that the compression observed in patient 1200012 was not consistent with collapse of the proximal end of the device (refer to Table 6.2-22 for additional details); nonetheless, the patient was counted as a failure for conservatism.

Beyond 30 days, there was one patient (1200006) who required placement of an additional stent-graft (described in Table 6.2-23) to treat an area of residual injury or possible endoleak (counted as a Miscellaneous/Other event between 31-365 days in Table 6.2-18).

Device Performance

The extent of injury healing, as determined by maximum transverse diameter at the site of injury, observed from the pre-procedure measurement to the 30-day, 6-month, and 12-month follow-up exams (based on core laboratory evaluation), is presented in Table 6.2-20. There were two patients (both at 6 months) who had an increase in diameter > 5 mm at the site of injury when compared to the pre-procedure measurement, which was associated with endoleak in one patient that required secondary intervention followed by conversion to open surgical repair in the setting of graft undersizing. There were no reports of endoleak or secondary intervention in the other patient, nor was there any change in size (< 5 mm change) when compared to the measurement at first follow-up.

Table 6.2-20. Aortic injury size and status based on results from core laboratory analysis

Follow-up*	Result
30-day	
Injury no longer visible (%, n/N)	76.7% (33/43)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)*	1.0 ± 2.3 (n=8, -2.4 – 4.6)
6-month	
Injury no longer visible (%, n/N)	88.2% (30/34)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)*	3.1 ± 3.4 (n=4, -0.3 – 6.3)[a,b]
12-month	
Injury no longer visible (%, n/N)	96.0% (24/25)
Max diameter change at site of injury (mm) (Mean ± SD, n, range)	-0.1 (n=1, -0.1)

*Max diameter change at the site of injury as compared to the pre-procedure measurement applied only if the injury was still visible at follow-up.

[a]Patient 1200058 – The max diameter increased > 5 mm at the site of injury when compared to the pre-procedure measurement; there was no change (≤ 5 mm change) when compared to the measurement at first follow-up. There were no reports of endoleak by the core lab and the patient has not undergone a secondary intervention.

[b]Patient 1200033 – The max diameter increased > 5 mm at the site of injury when compared to the pre-procedure measurement; the patient was reported to have an unknown endoleak type by the core laboratory (proximal Type I endoleak by the site), which required secondary intervention followed by conversion to open surgical repair in the setting of graft undersizing.

Endoleaks classified by type, as assessed by the core laboratory at each exam period, are reported in Table 6.2-21.

Table 6.2-21. Endoleak based on results from core laboratory analysis

Type	Percent Patients(number/total number)		
	30-day[a]	6-month	12-month
Any (new only)	7.1% (3/42)	0	0
Any (new and persistent)	7.1% (3/42)	2.9% (1/34)	0
Multiple	0	0	0
Proximal Type I	0	0	0
Distal Type I	0	0	0

Type	Percent Patients(number/total number)		
	30-day[a]	6-month	12-month
Type II	2.4% (1/42)[b]	0	0
Type III	0	0	0
Type IV	0	0	0
Unknown	4.8% (2/42)[c,d]	2.9% (1/34)[d]	0

[a]Endoleak was not assessed for 1 patient (1200012) due to a suboptimal exam submission (noncontrast exam).
[b]Patient 1200061
[c]Patient 1200035
[d]Patient 1200033 – Patient underwent secondary intervention as described further in Table 6.2-23.

No loss of patency was observed out to 12 months, as assessed by the core laboratory at 30 days. While not a loss in graft patency, one patient (1200060) required placement of an additional stent-graft at 435 days post-procedure (described in Table 6.2-23) to treat thrombus in the distal stent-graft and native aorta (counted as a Miscellaneous/Other event between 366-730 days in Table 6.2-18).

Table 6.2-22 reports device integrity findings based on the results from core laboratory analysis of follow-up imaging.

Table 6.2-22. Device integrity based on results from core laboratory analysis

Finding	Percent Patients (number/total number)		
	30-day	6-month	12-month
Kink	0	0	0
Device compression	2.3% (1/43)[a]	0	0
Device infolding	0	0	0
Stent fracture	0	0	0

[a] Patient 1200012 – Symmetrical compression occurred to the proximal section of the second component that was placed in this patient, due possibly to the component having been deployed through the distal suture loop of the proximal (first) component, which then restricted the second component from fully opening. This finding of compression is considered different from the compression/infolding due to hemodynamic forces commonly associated with the most proximal aspect of a stent-graft. The patient had not experienced any adverse sequelae, but underwent a secondary intervention 335 days post-procedure. Balloon angioplasty was performed and the secondary intervention was deemed successful. Core laboratory analysis of the secondary intervention angiogram revealed no device compression.

Tables 6.2-23 and 6.2-24 summarize the site-reported reasons for secondary intervention and types of secondary intervention, respectively. One patient underwent placement of screws for Type I endoleak. One patient underwent balloon angioplasty for device compression. Four patients underwent secondary interventions involving additional

stent-graft placement (one to treat dissection, one to treat a pseudoaneurysm, one to treat an area of residual injury or possible endoleak, and one to treat an area of thrombus).

Table 6.2-23. Site-reported reasons for secondary intervention

Reason	0-30 Days	31-365 Days	366-730 Days
Device compression	0	1[b]	0
Endoleak			
Type I proximal	1[a]	0	0
Type I distal	0	0	0
Type II	0	0	0
Type III (graft component overlap)	0	0	0
Type III (hole/tear in graft)	0	0	0
Type IV (through graft body)	0	0	0
Unknown	0	0	0
Clinical signs/symptoms	0	1[e]	0
Other	0	2[c,d]	1[f]

[a]Patient 1200033 – The patient was treated for a proximal Type I endoleak (per site assessment; core laboratory reported an unknown type of endoleak) 30 days post-procedure; the graft appeared undersized based on core laboratory-assessed aortic diameter measurements. Six Heli-FX™ screws were placed but the endoleak persisted and the secondary intervention was deemed unsuccessful. The patient later underwent conversion to open surgical repair 181 days after the index procedure. The patient survived the surgery and has not experienced any adverse events subsequent to the conversion as of 212 days post-procedure.

[b]Patient 1200012 underwent balloon angioplasty 335 days post-procedure to correct device compression of the proximal section of the second component (with no associated adverse sequelae) noted on the 1-month CT scan (refer to additional details in Table 6.2-22). The secondary intervention was deemed successful.

[c]Patient 1200024 underwent two secondary interventions following the index procedure. An unsuccessful secondary intervention (stent-graft placement) was attempted to treat a pseudoaneurysm proximal to the previously placed stent-graft (counted as a Vascular event in Table 6.2-18) on post-procedure day 74. On post-procedure day 79, the patient underwent a mini-sternotomy, aortic arch debranching, aortic bypass to the innominate and left carotid arteries with Hemashield™ graft, placement of a commercially available endograft, and bilateral chest tube placement to successfully treat the pseudoaneurysm. As described previously, the patient subsequently died on post-operative day 116. The death was adjudicated as procedure-related by the CEC (cause of death was exsanguination due to aortoesophageal fistula).

[d]Patient 1200006 underwent placement of a commercially available stent-graft 219 days post-procedure to treat an area of residual injury or possible endoleak (counted as a Miscellaneous/Other event in Table 6.2-18). The injury was incompletely treated during the index procedure due to the device having been placed too far distally (noted on the 6- month CT scan). The patient also required a left subclavian artery bypass. The secondary intervention was deemed successful.

[e]Patient 1200036 was diagnosed with an aortic dissection distal to the previously placed stent-graft (counted as a Vascular event in Table6.2-18) on post-operative day 286 after returning to the hospital for chest pain. The site noted that the patient was hypertensive and had stopped taking his blood pressure medication. An additional stent graft was placed the following day, which resolved the patient's symptoms. The patient was discharged 2 days after the reintervention.

[f]Patient 1200060 required placement of an additional stent-graft (overlapped with the existing graft) 435 days post-procedure to treat thrombus in the distal stent-graft and native aorta that was noted on the 12-month CT scan (counted as a Miscellaneous/Other event in Table 6.2-18). The site reported that the intervention was successful.

Table 6.2-24. Types of secondary interventions

Type*	0-30 Days	31-365 Days	366 – 730 Days
Percutaneous			
Additional proximal component	0	1[d]	1[f]
Balloon angioplasty	0	1[b]	0
Stent	0	2[c,e]	0
Other	0	0	0
Surgical			
Conversion to open repair	0	0	0
Other	1[a]	2[c,d]	0
Other	0	0	0

*A patient may have had more than one treatment type.
[a-f]Refer to footnotes in Table 6.2-23 for additional details.

Longer-term Follow-up

The information obtained > 30 days following endovascular repair appears consistent with results through 30 days with respect to morbidity, mortality, and device performance. The only event types observed during longer-term follow-up that were not previously observed within 30 days were aortic-injury-related death in one patient who developed an aortoesophageal fistula, aortic dissection distal to the endovascular graft in one patient who had stopped taking their blood pressure medications and was treated with placement of an additional endovascular graft component, and one patient who underwent conversion to open surgical repair due to the site-reported reason of proximal Type I endoleak in the setting of an undersized graft.

Summary

This study enrolled 50 patients treated with the Zenith Alpha™ Thoracic Endovascular Graft for BTAI. All but one patient received a single study component at the index procedure (one patient received two study components). One patient who received a single study component also received two commercially available components; the first study component and first commercial component placed were the same diameter and had been undersized as measurements were from a pre-procedure CT scan performed while the patient was not fully resuscitated, prompting additional labelling instruction that graft sizing for BTAI should be based on measurements in a fully resuscitated patient. All grafts were deployed successfully in the intended location, and all graft components were patent upon completion of deployment, yielding a technical success rate of 100%.

There was one death within 30 days of endovascular repair, which was adjudicated by an independent CEC as not related to the BTAI repair. There were no ruptures reported at any follow-up time point. There were no conversions to open repair within the first 30 days following the index procedure. Patients experienced adverse events in each of the organ system categories.

There were no core laboratory-identified Type I or Type III endoleaks, device migrations, device infolding, or stent fractures. One occurrence of device compression was noted without any adverse clinical sequelae, and resolved after a secondary intervention. One patient underwent successful conversion to open surgical repair 181 days post-procedure (due to a site-reported Type I endoleak that was the result of graft undersizing) and remained alive beyond 30 days following the conversion procedure. There was one aortic-injury-related death, which occurred greater than 30 days after the index procedure (in a patient with aortoesophageal fistula).

The results for the primary safety and effectiveness endpoints were within the expected ranges for treatment of patients with BTAI. Overall, the results provide a reasonable assurance of safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of BTAI.

6.3. Summary of Supplemental Clinical Information

6.3.1. Longer-term Follow-up (> 2 years) – Aneurysm/Ulcer Pivotal Study

As of April 7, 2015 there were 34 patients eligible for follow-up beyond 2 years (as shown in Table 6.1-2). Three patient deaths have been reported > 730 days following endovascular repair (2 of which were CEC-adjudicated as not related to TAA-repair and 1 which the CEC was unable to adjudicate). There are no reports of rupture or conversion to open surgical repair > 730 days. One additional patient experienced aneurysm growth (> 5 mm) after 2 years, which was associated with an inadequate landing zone length. There were no new reports of migration or Type I or III endoleak beyond 2 years. One new stent fracture was identified at 3 years, without adverse clinical sequelae. Three patients have undergone reintervention beyond 2 years, each of which was described previously due to having exhibited aneurysm growth within 2 years (one patient also had distal Type I endoleak and migration within 2 years, while another also had distal Type I endoleak within 2 years).

6.3.2. Continued Access – Aneurysm/Ulcer Indication

The results from patients treated during the continued access investigation of the aneurysm/ulcer indication (n = 18) were consistent with the results described for the pivotal study cohort, including one patient with aneurysm growth and Type I endoleak (at 6 months) that was associated with graft undersizing following initial treatment of the aneurysm with only a proximal component. Additionally, a portion of the patients enrolled in the continued access investigation (n = 11) were treated with the rotation handle version of the introduction system, which successfully deployed the stent-graft in all cases, consistent with the deployment results based on bench testing.

6.3.3. European Post-market Survey – Delivery System with Rotational Handle

A post-market survey was implemented in Europe to gather additional supportive information regarding clinical performance of the rotation handle introduction system. Physician users in Europe were surveyed on the procedural performance of the rotation handle system beginning March 31, 2014. A total of 38 surveys were completed as of June 30, 2014. Table 6.3.3-1 summarizes the survey results.

Table 6.3.3-1. Results of European post-market survey

Survey Question	Response Percent (number/total number)	
Did the introduction system with the rotation handle successfully retract the release-wires without the use of the alternate sequence?	Yes	100% (38/38)
	No	0
Was the alternate sequence successful in retracting the release-wires?	Yes	Not applicable
	No	Not applicable
	Not applicable	100% (38/38)
Was the graft successfully deployed in the intended location?	Yes	97.4% (37/38)
	No	2.6% (1/38)[a]
Was the graft patent at the completion of the procedure?	Yes	100% (38/38)
	No	0

[a]Slight distal migration of a tapered proximal component was reported.

All grafts were successfully deployed in the intended location using the primary release sequence, as described in the IFU, with the exception of one report of a slight distal migration during deployment. The alternate release sequence, which is also described in the IFU and is intended to be used in situations in which deployment difficulties involving the handle are encountered, was not used in any case. Furthermore, all grafts were patent at the completion of the procedure and no unique findings were observed as compared to the results from the pivotal clinical studies. These results in combination

with the results from the preclinical studies and uses of the introduction system with rotation handle during continued access provide a reasonable assurance of safety and effectiveness of the modifications that were made to the user interface since the time of enrollment completion in the pivotal clinical studies.