SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Endovascular Graft

Device Trade Name: Zenith® Iliac Branch

Device Procode: MIH

Applicant's Name and Address: William A. Cook Australia Pty. Ltd.
95 Brandl Street, Eight Mile Plains Queensland
4113, Australia

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P020018/S064

Date of FDA Notice of Approval: May 30, 2025

The original PMA for the Zenith Flex® AAA Endovascular Graft with Z-Trak Introduction System and Ancillary Components (P020018) was approved on 23 May 2003 and is indicated for the endovascular treatment of patients with abdominal aortic or aorto-iliac aneurysms having morphology suitable for endovascular repair.

The SSED to support the indication is available on the CDRH website and is incorporated by reference here. The current supplement was submitted to obtain premarket approval for the Zenith® Iliac Branch for use in conjunction with the Zenith Flex AAA Endovascular Graft or the Zenith Fenestrated Endovascular Graft in the treatment of patients with aortoiliac or iliac aneurysms.

II. INDICATIONS FOR USE

The Zenith® Iliac Branch, when used with the necessary additional components (Zenith AAA devices and a covered bridging stent), is indicated for endovascular treatment of aortoiliac or iliac aneurysms to preserve internal iliac arterial blood flow when the distal sealing site in the common iliac artery is insufficient for the AAA device alone and when the vessel morphology is suitable for repair, including:

- Common iliac artery diameter at the level of the internal iliac artery (luminal diameter) ≥16 mm
- Adequate iliac/femoral access compatible with a 20 French (7.7mm O.D.) introduction system
- Non-aneurysmal external iliac artery fixation segment distal to the aneurysm:
    - With a length of at least 20mm

    - With a diameter measured outer wall to outer wall of no greater than 11mm and no less than 8mm.
- Non-aneurysmal internal iliac artery segment distal to the aneurysm:
    - With a length of at least 10mm (with 20-30mm being preferred)
    - With a diameter measured outer wall to outer wall no greater than 10mm and no less than 7mm

III. CONTRAINDICATIONS

The Zenith® Iliac Branch is contraindicated in:

- Patients with known sensitivities or allergies to stainless steel, polyester, solder (tin silver) nitinol (nickel, titanium), polypropylene, urethane, gold or ePTFE.
- Patients with a systemic infection who may be at increased risk of endovascular graft infection.
- Patients with uncorrected bleeding disorders.
- Patients who cannot receive recommended antiplatelet and/or anticoagulation therapy.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Zenith® Iliac Branch labeling (Instructions for Use).

V. DEVICE DESCRIPTION

The Zenith® Iliac Branch (ZBIS) is intended to be used in conjunction with the Zenith Flex AAA Endovascular Graft (i.e., a Flex AAA main body and two iliac leg graft components) or Zenith® Fenestrated AAA Endovascular Graft (i.e., a fenestrated proximal body and a bifurcated distal body), Zenith Spiral-Z AAA Iliac Leg (ZSLE) and a bridging stent. The final configuration of the deployed endovascular components is provided in Figure 1.

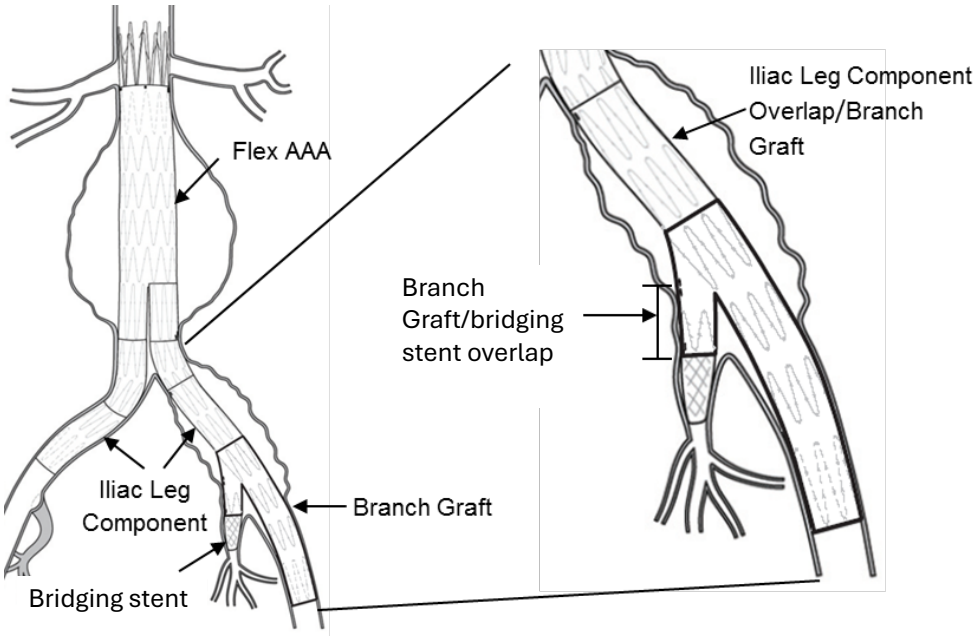

Figure 1. Final Configuration of the Zenith® Iliac Branch System

ZBIS Graft (implant)

The ZBIS is a bifurcated branch vessel graft with openings to connect the common iliac, internal iliac (sidebranch), and external iliac arteries (Figure 1 and Figure 2).
The graft is constructed of full-thickness, woven polyester fabric sewn to self-expanding stainless steel and nitinol Cook Z-Stents with braided polyester and monofilament polypropylene suture providing integrity and allowing exclusion of blood flow to the aneurysm and through the graft lumen. The graft is fully stented to provide stability and the expansile force necessary to open the lumen of the graft during deployment.
At the distal graft margin of the external iliac graft segment, the stainless-steel Z-Stent is attached to the inner lumen of the stent graft to achieve sealing with the vessel. Elsewhere, the Z-Stents are sutured on the external surface. The nitinol reinforcement rings are sutured to the most proximal graft edge, to the sidebranch proximal to the nitinol Z-Stent, and to the most distal aspect of the sidebranch. These rings help maintain lumen patency during access. Additionally, the Cook Z-Stents are intended to provide the necessary seal of the graft to the vessel wall (Figure 2). To facilitate fluoroscopic visualization of the stent graft, four radiopaque gold markers are positioned along the internal iliac side of the proximal portion of the graft to indicate the position of the sidebranch segment.

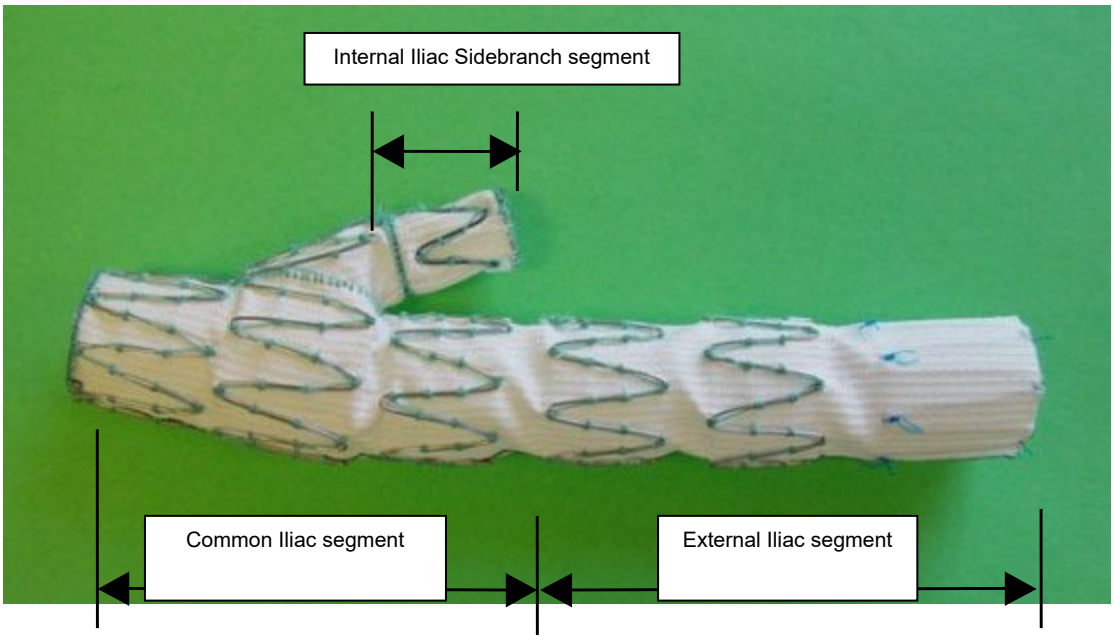

Figure 2. Zenith® Iliac Branch implant

Table 1 details the available lengths and diameters of the ZBIS. The component diameters should be selected as described in Table 1. The length of the ZBIS is chosen to extend from the proximal portion of the common iliac artery to the external iliac artery. 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 intraoperative flexibility to achieve optimal procedural outcomes.

Table 1. Zenith® Iliac Branch Size Matrix

Reorder number[a]	Proximal diameter mm	Distal diameter mm	Sidebranch diameter[b] mm	Introduction sheath		Iliac segment length		Total graft length mm
				French size Fr	(I.D. / O.D.) mm	Common mm	External mm	
ZBIS-10-45-41-US	12	10	8	20	(6.7 / 7.7)	45	41	86
ZBIS-10-61-41-US	12	10	8	20	(6.7 / 7.7)	61	41	102
ZBIS-10-45-58-US	12	10	8	20	(6.7 / 7.7)	45	58	103
ZBIS-10-61-58-US	12	10	8	20	(6.7 / 7.7)	61	58	119
ZBIS-12-45-41-US	12	12	8	20	(6.7 / 7.7)	45	41	86
ZBIS-12-61-41-US	12	12	8	20	(6.7 / 7.7)	61	41	102
ZBIS-12-45-58-US	12	12	8	20	(6.7 / 7.7)	45	58	103

Reorder number[a]	Proximal diameter mm	Distal diameter mm	Sidebranch diameter[b] mm	Introduction sheath		Iliac segment length		Total graft length mm
				French size Fr	(I.D. / O.D.) mm	Common mm	External mm	
ZBIS-12-61-58-US	12	12	8	20	(6.7 / 7.7)	61	58	119

[a]ZBIS-XX-YY-ZZ-US is the ZBIS where XX is distal diameter, YY is the Common Iliac Segment Length (length from the proximal graft edge to the tip of the internal iliac segment), and ZZ is the External Iliac Segment Length (length from the tip of the internal iliac segment to distal edge of the graft).
[b]Internal iliac segment contains a 6 mm diameter nitinol z-stent, but should be expanded to at least 8 mm during bridging stent system deployment.

The choice of ZBIS diameter is determined from the outer wall to outer wall vessel diameter and not the lumen diameter. Undersizing or oversizing may result in incomplete sealing or compromised flow. Table 2 is a sizing guide for the external iliac segment.

Table 2. Zenith® Iliac Branch Diameter Sizing Guide (External Iliac Segment)

Intended external iliac vessel diameter[a,b] mm	Branch external iliac leg diameter[c] mm	Introduction Sheath	
		French size Fr	(I.D. / O.D.) mm
8	10	20	(6.7 / 7.7)
9	10	20	(6.7 / 7.7)
10	12	20	(6.7 / 7.7)
11	12	20	(6.7 / 7.7)

[a]Maximum diameter along the distal fixation site.
[b]Round measured iliac diameter to nearest mm.
[c]Additional considerations may affect choice of diameter.
*All dimensions are nominal.

ZBIS Delivery System

The ZBIS is shipped pre-loaded onto the H&L-B One-Shot Introduction System (Figure 3). It has a sequential deployment method with built-in features to provide continuous control of the endovascular graft throughout the deployment procedure. The proximal end of the graft is attached to the delivery system by two nitinol trigger-wires. The distal end of the graft is also attached to the delivery system and held by an independent stainless-steel trigger-wire. The H&L-B One-Shot Introduction System enables precise positioning and allows readjustment of the final graft position before full deployment.
The delivery system uses a 20 Fr (6.7 mm I.D.) H&L-B One-Shot Introduction System that includes both a pre-loaded catheter, used to facilitate cannulation of the side branch, and wire guide, used to ensure that the lumen of the catheter is preserved during loading and shipping. The pre-loaded catheter is curved in order to enhance the positioning capability of the wire guide during the snaring process. All systems are compatible with a 0.035-inch (0.89 mm) wire guide.

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

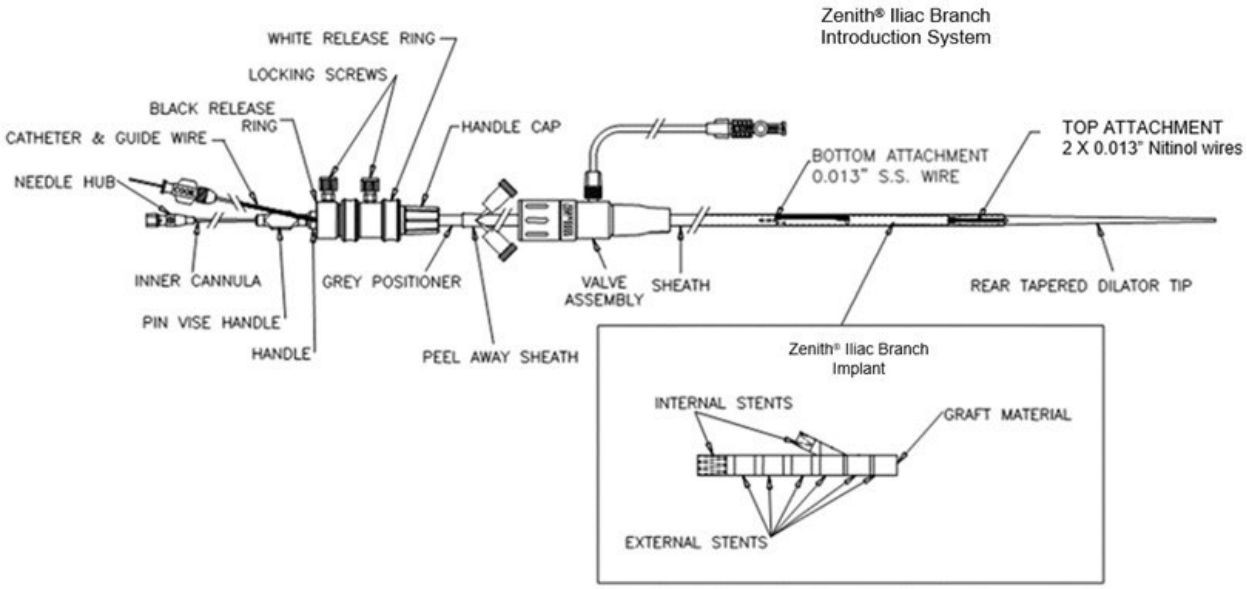

Figure 3. Zenith® Iliac Branch (implant) and H&L-B One-Shot Introduction System (delivery system)

Additional Components - Proximal Main Body, Iliac Leg, and Covered Stent

The Zenith® Iliac Branch (ZBIS) must be used with an appropriate Zenith proximal device (i.e., Zenith® Flex AAA Endovascular Graft (TFFB) or Zenith® Fenestrated AAA Endovascular Graft (ZFEN)), Zenith Spiral-Z AAA Iliac Leg (ZSLE), and appropriate bridging stent. The common iliac section of the Zenith® Iliac Branch, positioned in the common iliac artery, will be connected to the short (contralateral) limb of a Zenith proximal device (TFFB or ZFEN) by a ZSLE graft of suitable length and with a distal diameter of 16 mm (i.e., ZSLE-16-YY-ZT).

The Zenith® Iliac Branch has been studied with the Getinge iCAST covered stent as the bridging stent – see Sections IX and X below for non-clinical and clinical information on this device combination.

The Instructions for Use (IFU) for the Zenith® Iliac Branch includes information regarding required materials, patient selection, anatomical requirements, recommended device sizing, and the step-by-step implant procedure. Similar details are available in the IFU for each commercially available device listed in Table 2.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives used for the treatment of iliac or aortoiliac aneurysms, including endovascular repair using other iliac branched endovascular grafts, medical management, open surgical repair, or internal iliac artery coverage or occlusion. Each alternative has its own advantages and disadvantages. The physician should fully discuss these alternatives with the patient to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Zenith® Iliac Branch has been commercially available outside the United States since 2006. It was first marketed in the European Union and later commercialized in the Middle East/Africa, Asia, and South America. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) that may be associated with the use of the device:

- Allergic reaction and/or anaphylactoid response to x-ray contrast dye, anti-platelet therapy, device materials
- 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
- 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, 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
- Endoprosthesis: improper component placement; incomplete component deployment; component migration; suture break; occlusion; infection; stent fracture; graft material wear; dilatation; erosion; puncture; endoleak; barb separation and corrosion

- Fever and localized inflammation
- Genitourinary complications and subsequent attendant problems (e.g., ischemia, erosion, fistula, incontinence, hematuria, infection)
- Graft or native vessel occlusion
- 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)
- Multi-system organ failure
- Neurologic local or systemic complications and subsequent attendant problems (e.g., stroke, transient ischemic attack, paraplegia, paraparesis, paralysis)
- Post-implant syndrome
- 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
- Vessel damage
- Wound complications and subsequent attendant problems (e.g., dehiscence, infection)
- Vascular spasm or vascular trauma (e.g., iliofemoral vessel dissection, bleeding, rupture, death)

For the specific adverse events that occurred in the clinical study, please see Section X, *Safety and Effectiveness Results* below.

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Biocompatibility Testing

A thorough panel of biocompatibility testing was performed on the Zenith® Iliac Branch and delivery system in accordance with ISO 10993-1, *Biological evaluation of medical devices – Part 1: Evaluation and testing*, the FDA Guidance for Industry and Food and Drug Administration Staff, *Use of International Standard ISO 10993-1, Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process* (September 2023), and 21 CFR 58 Good Laboratory Practice (GLP) requirements. Specifically, the Zenith® Iliac Branch was assessed by tests considered appropriate for devices categorized as an implant medical device contacting blood for long term contact duration (i.e., > 30 days). The H&L-B One-Shot Introduction System (delivery system) was assessed by tests considered appropriate for devices categorized as an external communicating medical device contacting circulating blood for limited contact duration (i.e., ≤ 24 hours).

Tables 3 summarizes the test results for the Zenith® Iliac Branch (implant) and H&L-B One-Shot Introduction System (delivery system). The biocompatibility test results demonstrate that the Zenith® Iliac Branch (implant) and H&L-B One-Shot Introduction System (delivery system) are safe and acceptable for clinical use.

Table 3. Biological testing supporting the biological safety of the ZBIS (implant) and H&L-B One-Shot Introduction System (delivery system)

Biological Evaluation	Test Purpose	Acceptance Criteria	Results
ZBIS (Implant)			
Cytotoxicity *MEM Elution Test*	Determine the potential for the test article to cause cytotoxicity	The test article met the requirements of the test if the biological response was ≤ grade 2 (mild).	**NON-CYTOTOXIC**
Sensitization *Magnusson and Kligman Maximization Test*	Investigate the potential for delayed dermal contact sensitization	None of the test extract injection sites show a greater biological reaction than the control injection sites, with the difference in mean scores for test and control being ≤ 1.0.	**NON-SENSITIZER**
Irritation *Intracutaneous Injection Test*	Determine if the test article causes local dermal irritation following intracutaneous injection in rabbits	None of the test extract injection sites show a greater biological reaction than the control injection sites, with the difference in mean scores for test and control being ≤ 1.0.	**NON-IRRITANT**
Acute Systemic Toxicity *Systemic Injection*	Determine if the test article causes systemic toxicity following injection in mice	The test article met the standard requirements if treated animals did not show significantly greater reactions than control animals, but failed if two or more animals died, displayed abnormal behavior, or if three or more animals experienced body weight loss over 2 grams.	**NON-TOXIC**
Pyrogenicity *Rabbit Pyrogen Test (Material Mediated)*	Determine if the test article induces a pyrogenic response following intravenous injection in rabbits	If no individual animal exhibited a temperature increase of 0.5°C or more above its baseline, the extract was considered nonpyrogenic.	**NON-PYROGENIC**

Biological Evaluation	Test Purpose	Acceptance Criteria	Results
Systemic Toxicity *Subcutaneous Implantation, 13 Weeks*	Determine the potential for systemic toxicity of the test article following subcutaneous implantation in the rat for up to 13 weeks.	The test and control groups were compared using separate analyses for male and female animals, evaluating body weight, organ weight, ratios, hematology, and clinical chemistry with parametric or nonparametric tests, considering *p*-values < 0.05 as statistically significant.	**MINIMAL TO NO LOCAL REACTION and NON-TOXIC**
Genotoxicity *Bacterial Reverse Mutation*	Evaluate the mutagenic potential of the test article (or its metabolites) by measuring its ability to induce back mutations at selected loci of several strains of bacteria in the presence and absence of microsomal enzymes.	A test is considered positive for strains TA98, TA100 and WP2*uvrA* when there is a 2-fold or greater increase in the number of revertant colonies, or a 3-fold increase in revertants for strains TA1535 and TA1537 when compared to the controls.	**NON-GENOTOXIC**
Genotoxicity *Mouse Lymphoma Assay*	Determine the ability of a test article to induce forward mutations at the thymidine kinase (TK) locus as assayed by colony growth of L5178Y mouse lymphoma cells.	The test article was considered mutagenic if a two-fold or greater increase in mutant frequency of the L5178Y/$TK^{+/-}$ cell line over the negative control was observed.	**NON-GENOTOXIC**
Implantation *Local Tissue Response, 4 Weeks*	Determine if the test article causes a local tissue response after 4 weeks implantation into muscle tissue of rabbits	A microscopic evaluation of representative implant sites from each rabbit was conducted, grading cellular changes on a severity scale of 0 to 4 and compared to the control. A difference in scores up to 0.5 is considered not significant.	**MINIMAL TO NO LOCAL REACTION**
Implantation *Local Tissue Response, 12 Weeks*	Determine if the test article causes a local tissue response after 12 weeks implantation into muscle tissue of rabbits		**MINIMAL TO NO LOCAL REACTION**
Hemocompatibility *Hemolysis – Direct and Extract*	Determine if the test article causes hemolysis	The mean blank corrected % hemolysis above the negative control of the test article must be < 2 % to be non-hemolytic.	**NON-HEMOLYTIC**
Hemocompatibility *Complement Activation*	Evaluate the test article's potential to activate the C3a and SC5b-9 complement system	The concentration of C3a and SC5b-9 in the test article must not be significantly higher than in the untreated or negative control plasma.	**NOT A COMPLEMENT ACTIVATOR**
Hemocompatibility *Platelet Leukocyte Count*	Evaluate the test article's potential to activate or damage platelets and leukocytes.	The test article passes if the test article platelet mean percentage value is between 80 to 120% and the test article platelet mean percentage value is at least 30% above the positive control.	**NON-THROMBOGENIC**

Biological Evaluation	Test Purpose	Acceptance Criteria	Results
Hemocompatibility *Partial Thromboplastin Time (PTT)*	Determine the potential induction of coagulation of human plasma via measurement of the PTT in response to the test article.	The test article or Sponsor Provided Control (SPC) was considered to pass if the final average clotting time of the test article or SPC was not statistically lower than either the negative reference material or the negative control.	**NON-THROMBOGENIC**
Carcinogenicity	The patient contacting materials in the ZBIS graft underwent a thorough qualitative risk assessment, and biocompatibility testing included 13-week systemic toxicity testing in rats, and genotoxicity testing through bacterial reverse mutation and mouse lymphoma assays, confirming the absence of potent systemic toxicants and genotoxic carcinogens. Additionally, all patient-contacting materials and processing aids were evaluated and found to have been used in other devices under this PMA which were previously evaluated for systemic toxicity and carcinogenicity, ensuring negligible risks of systemic toxicity and carcinogenicity.	In adult patient populations, demonstration of acceptable margins of safety (MOS) and TTC evaluations for all exhaustively extractable chemical groups and chemicals from the test article.	**ACCEPTABLE**
Reproductive and Developmental Toxicity			
H&L-B OneShot Introduction System (Delivery System)			
Cytotoxicity *MEM Elution Test*	Determine the potential for the test article to cause cytotoxicity	The test article met the requirements of the test if the biological response was ≤ grade 2 (mild).	**NON-CYTOTOXIC**
Sensitization *Magnusson and Kligman Maximization Test*	Investigate the potential for delayed dermal contact sensitization	None of the test extract injection sites show a greater biological reaction than the control injection sites, with the difference in mean scores for test and control being ≤ 1.0.	**NON-SENSITIZER**

Biological Evaluation	Test Purpose	Acceptance Criteria	Results
Irritation *Intracutaneous Injection Test*	Determine if the test article causes local dermal irritation following intracutaneous injection in rabbits	None of the test extract injection sites show a greater biological reaction than the control injection sites, with the difference in mean scores for test and control being ≤ 1.0.	**NON-IRRITANT**
Acute Systemic Toxicity *Systemic Injection*	Determine if the test article causes local dermal irritation following injection in mice	The test article meets the requirements if treated animals do not exhibit significantly greater biological reactivity than control animals, and if no group of five animals experiencing two or more deaths, abnormal behavior in two or more animals, or body weight loss exceeding 10%.	**NON-TOXIC**
Pyrogenicity *Rabbit Pyrogen Test (Material Mediated)*	Determine if the test article induces a pyrogenic response following intravenous injection in rabbits	If no individual animal exhibited a temperature increase of 0.5°C or more above its baseline, the extract was considered nonpyrogenic.	**NON-PYROGENIC**
Hemocompatibility *Hemolysis – Direct and Extract*	Determine if the test article causes hemolysis	The mean blank corrected % hemolysis above the negative control of the test article must be < 2 % to be non-hemolytic.	**NON-HEMOLYTIC**
Hemocompatibility *Complement Activation*	Evaluate the test article's potential to activate the C3a and SC5b-9 complement system	The concentration of C3a and SC5b-9 in the test article must not be significantly higher than in the untreated or negative control plasma.	**NOT A COMPLEMENT ACTIVATOR**
Hemocompatibility *Platelet Leukocyte Count*	Evaluate the test article's potential to activate or damage platelets and leukocytes.	The test article passes if the test article platelet mean percentage value is between 80 to 120% and the test article platelet mean percentage value is at least 30% above the positive control.	**NON-THROMBOGENIC**
Hemocompatibility *Partial Thromboplastin Time (PTT)*	Determine if the placement of the test article would cause thrombosis during simulated clinical use	The test article or Sponsor Provided Control (SPC) was considered to pass if the final average clotting time of the test article or SPC was not statistically lower than either the negative reference material or the negative control.	**NON-THROMBOGENIC**

The Zenith® Iliac Branch has not been fully evaluated to establish potential for chronic toxicity and carcinogenicity. Prolonged exposure to systemic or carcinogenic toxicants may lead to long term tissue harm and long-term carcinogenic effects. The risks of these potential harms from this specific product have not been established. However, the available information from clinical use and animal study data appropriately leveraged from the previously approved Zenith components on with identical materials does not suggest chronic toxicity or carcinogenicity concerns.

B. Animal Studies

No animal testing was conducted on the Zenith® Iliac Branch. Information from clinical use and animal study data from the previously approved Zenith components was appropriately leveraged based on the similarities in the device design and materials. Additionally, a validated bifurcated iliac animal model is not available to address delivery and deployment. These attributes were assessed in simulated use testing, as described below.

C. Non-clinical Bench Testing

Comprehensive non-clinical bench testing was conducted as part of the design verification and validation to support the safety and effectiveness of the Zenith® Iliac Branch (ZBIS) and is summarized in Table 4. The test plan was developed in accordance with appropriate guidance documents and international standards, including FDA's Guidance for Industry and Staff*, Non-clinical tests and recommended labeling for intravascular stents and associated delivery systems* (2005, 2010, supplemented in 2015), and ISO 25539-1, *Cardiovascular implants – Endovascular devices – Part 1: Endovascular Prostheses*. All testing was conducted on devices representative of the final device intended for commercial use. The Zenith® Iliac Branch was evaluated with appropriate Zenith AAA proximal components and the Getinge iCAST™ Covered Stent System as the bridging stent. The test results verified that the Zenith® Iliac Branch met product performance and design specifications. Table 4 indicates which tests were performed on both non-aged and aged devices to support the product shelf life.

Table 4. Summary of Non-clinical Bench Testing for the Zenith® Iliac Branch

Test	Test Purpose	Acceptance Criteria	Results
Dimensional verification of the endovascular system*	Characterize the largest diameter encountered along the section of the delivery system to be inserted into the vasculature.	Delivery system nominal outer diameter shall be ≤ 7.7 mm. Length of sheath must be ≥ 30 +1/- 1.5 cm.	**PASS**
Force to Deploy*	Evaluate the force required to deploy and withdraw the ZBIS in a clinically relevant anatomical model.	The maximum force to deploy and withdraw the ZBIS will meet design requirements.	**PASS**
Delivery System Tensile Bond Strength*	Establish the tensile bond strength of delivery system joints and verify that the strength of the bond joints is adequate for the intended use	The tensile bond strength of delivery system bonds will meet design requirements.	**PASS**
Delivery System Torsional Bond Strength*	Establish the torsional bond strength of delivery system joints and verify that the strength of the bond joints is adequate for the intended use	The torsional bond strength of delivery system bonds will meet design requirements.	**PASS**
Simulated Use - Deployment accuracy*	Confirm delivery, deployment, and retraction of the ZBIS under simulated use conditions.	ZBIS shall be deployed within a representative anatomical model in accordance with the IFU.	**PASS**

Test	Test Purpose	Acceptance Criteria	Results
Hemostasis	Measure leak flow through a physiologically pressurized test article.	Fluid loss from the Captor valve shall be ≤ the fluid loss from the valve on the existing commercially available Zenith AAA endovascular graft delivery system.	**PASS**
Visibility	Evaluate the visibility of the ZBIS/iCAST and the delivery system under fluoroscopy.	The device must be visible under fluoroscopy.	**PASS**
ZBIS (implant)			
Corrosion	Evaluate the corrosion resistance of metallic components in the ZBIS and iCAST.	Corrosion must not affect the functional integrity of the implant.	**PASS**
Fatigue and Durability (FEA)	Evaluate longitudinal and pulsatile fatigue performance of ZBIS and iCAST stents for 400 million cycles (equivalent to 10 years).	Analyses must result in a fatigue safety factor > 1.0	**PASS**
Pulsatile Fatigue and Durability	Assess the fatigue durability of ZBIS and iCAST through exposure to time-accelerated, physiologically modeled, controlled displacement pulsatile loading through 400 million cycles (equivalent to 10 years).	The devices must withstand loading conditions and there must be no clinically relevant material wear, abrasion, or stent fracture.	**PASS**
Axial Fatigue and Durability	Assess durability of compressive and tensile forces along the longitudinal axis of the ZBIS and iCast to evaluate its durability and structural integrity over 400 million cycles (equivalent to 10 years).	The devices must withstand loading conditions and there must be no clinically relevant material wear, abrasion, or stent fracture.	**PASS**
Separation force for overlapping endovascular prostheses	Establish the forces required to separate the modular components of an endovascular graft prosthesis or to separate overlapping endoprostheses in the deployed state.	The force required to separate the overlapping components must be greater than the force induced by blood flow, acting on those components. • The force required to separate the bifurcated graft from the iliac leg graft must be > 1.7 N • The force required to separate the balloon expandable covered bridging stent from the internal iliac branch must be > 0.8 N.	**PASS**
Radial force (self-expanding endovascular prostheses)	Demonstrate that when grafts are sized correctly, the z-stents are expected to exert a radial force sufficient to maintain graft patency and apposition to the vessel wall without causing vessel damage	The radial force for each stent will meet design requirements.	**PASS**

Test	Test Purpose	Acceptance Criteria	Results
Resistance to kinking (flexibility)	Determine the minimum radius that the endovascular prosthesis can accommodate without kinking.	Graft body components must have a kink radius ≤ 34.7 mm	**PASS**
Integral Water Permeability	Assess the integral water permeability of a test article.	Permeability of graft material after the addition of sutures should not be greater than 550 mL/min/cm^2.	**PASS**
Dimensional verification of the endovascular prosthesis*	Evaluate the final stent dimension and ensure design specifications were met.	The graft diameters and lengths meet device specifications.	**PASS**
Burst strength	Determine the circumferential tensile strength of a tubular test article.	Circumferential tensile strength of the graft material must be ≥ 2.7 N/mm.	**PASS**
Factory anastomotic strength (endovascular grafts with seams in the graft material)	Evaluate the durability and integrity of the device seams to withstand the forces encountered during implantation and long-term use.	Circumferential tensile strength of the graft material seam must be ≥ 1.7 N/mm.	**PASS**
Longitudinal tensile strength	Assess the ability of the device to withstand tension and measure its maximum strength before breaking or deforming.	The longitudinal tensile strength of the implant fabric must be > 100 N.	**PASS**
MRI safety and compatibility	To evaluate the MRI safety and compatibility	The measured magnetically induced deflection force and torque shall be < 29.4 N/cm^2. The measured RF induced temperature rise shall be appropriately low as to not induce tissue damage. The measured magnetically induced force shall be less than the force required to cause the device to separate.	**PASS**

Note: The specific engineering tests completed to support the two-year shelf life for the ZBIS are denoted by an asterisk (*).

D. Sterilization, Packaging and Shelf Life

The Zenith® Iliac Branch is sterilized by a validated Ethylene Oxide (EtO) sterilization process to achieve a minimum Sterility Assurance Level (SAL) of 10^{-6}. The methods used to validate the sterilization cycle are in accordance with ISO 11135-1, "*Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of sterilization process for medical devices."* Additionally, the EO residual and bacterial endotoxin was verified to be within acceptable ranges in accordance with ISO 10993-7 "*Biological Evaluation of Medical Devices – Part 7: Ethylene Oxide Sterilization Residuals*."

Product and packaging testing of the Zenith® Iliac Branch was performed and validated to support the device's 2-year shelf life. The packaging was demonstrated to protect the product and to maintain a sterile barrier through simulated distribution and shelf life. Non-clinical functional testing of the device after aging was performed as indicated in Table 4. Together, the data supports a 2-year shelf life for the Zenith® Iliac Branch.

X. SUMMARY OF THE PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of endovascular treatment with the Zenith® Iliac Branch (formerly branded under the clinical investigation as the Zenith Branch Endovascular Graft-Iliac Bifurcation) in combination with the Getinge iCAST™ Covered Stent System (formally branded as the Atrium iCAST Covered Stent and referred herein as the iCAST stent) for the treatment of patients with aortoiliac or iliac aneurysms. The clinical study was conducted in the United States under an Investigational Device Exemption (IDE# G070241; NCT02571907). Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The PRESERVE-Zenith Iliac Branch Clinical Study (conducted under the previous brand name PRESERVE Zenith Branch Endovascular Graft-Iliac Bifurcation Clinical Study) was a prospective, non-randomized, single-arm, multi-center clinical study intended to assess the safety and effectiveness of endovascular treatment with the ZBIS in combination with the iCAST stent for the treatment of patients with aortoiliac or iliac aneurysms with an unsuitable distal sealing site for a Zenith iliac leg component proximal to the common iliac bifurcation to maintain internal iliac artery patency during endovascular aneurysm repair.

A total of 40 patients were treated with ZBIS and iCAST between 01 April 2014 and 06 May 2015. The database for this PMA reflects data locked on 10 February 2021. Study patients were enrolled across 18 investigational sites in the United States.

This study evaluated safety and effectiveness through comparison to performance goals. The primary endpoint was 6-month freedom from patency-related intervention of the Internal Iliac Artery (IIA) (further defined below). The performance goal for the primary endpoint was established through a review of data from reports on the complications rates associated with coil embolization and stent graft coverage of the IIA in endovascular repair of aortoiliac aneurysms. The secondary safety endpoint was 30-day freedom from morbidity (i.e., the morbidity index defined below). The performance goal for the secondary safety endpoint was established through a review of safety data from the Zenith AAA Endovascular Graft Clinical Study (P020018). The secondary effectiveness endpoint for the study was branch vessel patency at 6 months. This endpoint was assessed for descriptive purposes only and therefore a performance goal for this endpoint was not established.

An independent data safety monitoring board (DSMB) monitored the clinical trial according to an established safety monitoring plan. An independent clinical events committee (CEC) adjudicated predefined clinical events reported during the study in accordance with the CEC charter. An independent core laboratory analyzed all patient imaging.

1. Clinical Inclusion and Exclusion Criteria

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

1) An aortoiliac or iliac aneurysm
2) An unsuitable distal sealing site for a Zenith iliac leg graft within the common iliac artery on the intended side of ZBIS implantation (e.g., fixation/seal length < 10 mm or diameter > 20 mm)

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

General Exclusion Criteria

1) Age < 18 years
2) A medical condition or disorder that may limit life expectancy to less than 2 years or that may cause non-compliance with the protocol
3) Pregnant, breast-feeding, or planning on becoming pregnant prior to completion of the study
4) Unwilling or unable to comply with the follow-up schedule
5) Unable or unwilling to give informed consent
6) Simultaneously participating in another investigative device or drug study (patient must have completed the follow-up phase for the primary endpoint of any previous study at least 30 days prior to enrollment in this study)

Medical Exclusion Criteria

1) Pre-procedure creatinine > 2.0 mg/dl and not on dialysis (patient must be able to undergo contrast-enhanced CT)
2) Cultural objection to receipt of blood or blood products
3) Known hypersensitivity or contraindication to study device materials (i.e., stainless steel, polyester, polytetrafluoroethylene, gold, or nitinol)
4) Known hypersensitivity or contraindication to contrast material that, in the opinion of the investigator, cannot be adequately premedicated
5) Leaking, ruptured, or symptomatic aneurysm
6) Uncorrectable coagulopathy
7) Systemic infection (i.e., sepsis)
8) Previous treatment (e.g., endovascular or surgical AAA graft, stents in the common iliac artery or external iliac artery) below the aortic bifurcation that precludes the use of the Zenith Branch Endovascular Graft-Iliac Bifurcation
9) Previously placed stent in internal iliac artery on side of intended implantation
10) Planned significant interventional or surgical procedure that is unrelated to AAA repair within 30 days before or after AAA repair

Anatomical Exclusion Criteria

Patients were excluded from the study if they were unsuitable for implantation of a Zenith Flex AAA Endovascular Graft (physicians will determine suitability of a patient based on their clinical experience) or if any of the following are true:

On the intended side of ZBIS implantation:

1) A non-aneurysmal external iliac segment (fixation site) distal to the aneurysm:
    a. with a length of < 20 mm, or
    b. with an outer wall diameter < 8 mm
2) Common iliac artery length < 50 mm
3) Occluded or > 50% stenosed internal iliac artery
4) Aneurysmal disease distal to intended internal iliac artery landing zone
5) A non-aneurysmal main internal iliac artery trunk segment (fixation site):
    a. with a length of < 10 mm, or
    b. with an inner wall diameter > 10 mm or < 7 mm
6) Common iliac artery diameter at the level of the internal iliac artery (luminal) < 16 mm

On the side opposite of intended ZBIS implantation**:**

1) Inadequate common iliac fixation for a Zenith iliac leg graft
2) > 70% stenosis of the internal iliac artery (unresolved at the time of index procedure)

[Note: These criteria for the side opposite of intended ZBIS implantation did not apply if the patient was considered unsuitable for open surgical repair in the opinion of the investigator, in which case the investigator could treat the side opposite of intended ZBIS implantation per standard practice.]

On either the intended or the opposite side of ZBIS implantation:

1) Significant occlusive disease, tortuosity, or calcification of the iliac arteries
2) Unsuitable arterial anatomy (e.g., excessive angulation between the internal and common/external iliac arteries)

2. Follow-up Schedule

Prior to the study procedure, patients underwent a clinical exam, blood test, and CT scan. Postoperatively, patients were scheduled to return for follow-up examinations within 7 days (pre-discharge), at 30 days, 6 months, 12 months, and then annually through 5 years postoperatively. The objective parameters measured during the study based on CT included assessment of endoleaks, migration, patency, and device integrity. Adverse events and complications were recorded at all visits. The key timepoints and data collection information are shown in Table 5.

Table 5. Data Collection Schedule for the PRESERVE Clinical Study

Data Collection	Pre-op	Intra-op	Pre-discharge	Month						
				1	6	12	24	36	48	60
CT Scan[a]	X			X[b]	X[b]	X[b]	X[b]	X[b]	X[b]	X[b]
Angiography	X[c]	X								
Blood tests[d]	X		X	X	X	X	X	X	X	X
Clinical Exam	X		X	X	X	X	X	X	X	X

[a] Selective angiography may have been performed to provide more focused imaging in instances potential device integrity issues were identified but unable to be confirmed on CT.
[b] In patients experiencing renal failure during follow-up, selective angiography (preferred) or duplex ultrasound may have been used in conjunction with non-contrast CT.
[c] Pre-procedure angiography may have been requested at discretion of film reviewer/proctor.
[d] Blood tests included creatinine.

3. Clinical Endpoints

Primary Endpoint
With regards to safety and effectiveness, the primary endpoint for the study was the assessment of 6-month freedom from patency-related intervention. Freedom from patency-related intervention was defined as freedom from a secondary intervention to treat a > 60% stenosis of the internal iliac artery (IIA; as identified through computed tomography [CT] scan, angiography, or duplex ultrasound and confirmed by core laboratory) associated with clinical symptoms. This endpoint definition includes patients with internal iliac artery stenosis following successful placement of the ZBIS and covered bridging stent, and any cases of technical failure resulting in occlusion of the internal iliac artery during the initial implant procedure that require secondary intervention for associated clinical symptoms.

For the power calculation of the primary hypothesis, the true patency rate of the IIA following treatment with the ZBIS was assumed to be 83% based on clinical literature describing outcomes associated with sacrificing the IIA during endovascular repair available at the time of protocol development. A performance goal of 55% for freedom from patency-related intervention was determined and a simulation study indicated that a maximum sample size of 25 patients would provide a power of approximately 88.5%, at a type I error rate of 2.5%.

The analysis required that the performance goal of 55% be met (H_0: $\pi \leq 55\%$; H_a: $\pi > 55\%$). The study device was considered to have met the primary endpoint if the 2.5^{th} percentile of the Bayesian posterior distribution of π was greater than the performance goal.

Secondary Safety Endpoint
The secondary safety endpoint for the study was freedom from 30-day morbidity (i.e., the morbidity index, a measure of 33 elements in seven categories [i.e., cardiovascular, pulmonary, renal, bowel, wound, neurologic, and vascular]) and was associated with prospective power calculations and associated hypothesis testing. For the secondary safety hypothesis, the true rate of freedom from 30-day morbidity was assumed to be 72.5%, which was derived from patients with patent IIA in the Zenith AAA Endovascular

Graft Clinical Study who were free from 30-day morbidity (i.e., free from all 31 events in the Zenith AAA Endovascular Graft Clinical Study morbidity index [defined below] and hip/thigh/buttock claudication). With a performance goal of 46% for freedom from 30-day morbidity, the simulation study indicated that a maximum sample size of 29 patients would provide a power of 85.8%, at a type I error rate of 2.5%.

The analysis required that the performance goal of 46% be met (H_0: $p \leq 46\%$; H_a: $p > 46\%$). The study device was considered to have met the secondary endpoint if the 2.5^{th} percentile of the Bayesian posterior distribution of p was greater than the performance goal.

Additional Endpoints
Additional endpoints were evaluated including assessments of aneurysm-related death, conversion, rupture, 6-month branch vessel patency, success measures (i.e., technical success during the implant procedure, procedural success within 30 days, and treatment success at 12-month follow-up), clinical utility measures [i.e., duration of intensive care unit (ICU) stay, days to ambulation, days to resumption of oral fluid intake, days to resumption of regular diet, days to first bowel function, days to hospital discharge, blood replacement requirements], adverse events related to the ZBIS or iCAST stent, distal Type I endoleaks, and Type III endoleaks involving the ZBIS and iCAST stent. Summary statistics for these endpoints are provided, but no statistical inference or hypothesis testing was be performed.

B. Accountability of PMA Cohort

Enrollment in the study totaled 40 patients. Follow-up availability through 5 years is reported in Figure 1 and includes the number of patients eligible at each follow-up time point and the number of patients for whom clinical data were available.

Importantly, nearly all eligible patients (97.5%; 39/40) remained in the study at their 6-month follow-up visit which was the timepoint for the primary study endpoint. The percentage of eligible patients who completed the clinical exam and CT imaging was above 80% and above 75%, respectively, at each timepoint throughout the study. The number of patients available for analysis at each time point is shown in Table 6.

Table 6. Follow-up data availability - Pivotal Cohort (Through 5 Years)

Visit	Eligible for Follow-up	Percent of Data Available		Adequate Imaging for Core Laboratory to Assess Parameter					Events Occurring Before Next Interval			
		Clinical Exam	CT	Size Increase	Endoleak	Patency	Migration	Device Integrity	Death	Conversion	Lost to Follow-up (LTF)	Withdrawal
Procedure	40	N/A	N/A	N/A	92.5% (37/40)	92.5% (37/40)	N/A	N/A	0	0	0	0
Pre-discharge	40	100% (40/40)	N/A	N/A	N/A	N/A	N/A	N/A	0	0	0	0
1-month	40	100% (40/40)	100% (40/40)	N/A	100% (40/40)	100.0% (40/40)	N/A	97.5% (39/40)	1	0	0	0
6-month	39	94.9% (37/39)	94.9% (37/39)	94.9% (37/39)	94.9% (37/39)	94.9% (37/39)	94.9% (37/39)	92.3% (36/39)	0	0	2	0
12-month	37	100% (37/37)	100% (37/37)	100.0% (37/37)	97.3% (36/37)	97.3% (36/37)	100% (37/37)	100% (37/37)	0	0	0	0
2-year	37	86.5% (32/37)	75.7% (28/37)	75.7% (28/37)	73.0% (27/37)	78.4% (29/37)	75.7% (28/37)	75.7% (28/37)	0	0	0	2
3-year	35	88.6% (31/35)	88.6% (31/35)	88.6% (31/35)	82.9% (29/35)	94.3% (33/35)	88.6% (31/35)	88.6% (31/35)	1	0	0	1
4-year	33	81.8% (27/33)	84.8% (28/33)	84.8% (28/33)	87.9% (29/33)	87.9% (29/33)	84.8% (28/33)	81.8% (27/33)	2	0	1	0
5-year	30	90.0% (27/30)	86.7% (26/30)	86.7% (26/30)	83.3% (25/30)	83.3% (25/30)	86.7% (26/30)	86.7% (26/30)	N/A	N/A	N/A	N/A

Note: In patients experiencing renal failure and unable to undergo contrast-enhanced CT scan, a duplex ultrasound may be used in conjunction with noncontrast CT scan. In these cases, the core laboratory may be able to adequately assess aneurysm size change, endoleak, and patency when an ultrasound is performed in combination with a noncontrast CT scan.
N/A = Not applicable.

C. Study Population Demographics and Baseline Parameters

The demographics and baseline parameters of the study population are typical for a study of patients with extensive AAA disease involving the iliac arteries performed in the US.

Demographics

The demographics and patient characteristics, including age, sex, race, height, and weight are presented in Table 7. The mean age was 67.8 ± 9.0 years, with most patients being male (95.0%, 38/40) and of white ethnicity (87.5%, 38/40).

Table 7. Demographics and patient characteristics

Demographic	Mean ± SD (n, range) or Percent Patients (number/total number)
Age (years)	67.8 ± 9.0 (40, 48 – 86)
Sex	
Male	95.0% (38/40)
Female	5.0% (2/40)
Self-reported Race	
American Indian or Alaska Native	0% (0/40)
Asian	2.5% (1/40)
Black or African American	7.5% (3/40)
Hispanic or Latino	2.5% (1/40)
Native Hawaiian or other Pacific Islander	0% (0/40)
White	87.5% (35/40)
Height (in)	69.5 ± 2.7 (40, 64 – 76)
Weight (lbs)	198.4 ± 43.2 (40, 132.0 – 334.4)
BMI	28.8 ± 5.4 (40, 18.6 – 47.3)

Medical History and Comorbidities

Patient pre-existing comorbid medical conditions are summarized in Table 8. Common comorbidities in the population included hypertension (77.5%, 31/40) and past or current smoking (75%, 30/40).

Table 8. Medical history and comorbid conditions

Medical History	Percent Patients (number/total number)
Cardiovascular	
Myocardial infarction (MI)	25.0% (10/40)
Percutaneous transluminal coronary angioplasty (PTCA)/stent	17.5% (7/40)
Coronary artery bypass graft surgery (CABG)	17.5% (7/40)
Symptomatic congestive heart failure (CHF)	5.0% (2/40)
Angina	12.5% (5/40)
Cardiac arrhythmia	17.5% (7/40)

Medical History	Percent Patients (number/total number)
Vascular	
Thromboembolic event	5.0% (2/40)
Peripheral vascular disease	5.0% (2/40)
Aneurysm (not subject of current study)	30.0% (12/40)
Dissection	0% (0/40)
Thoracic trauma	0% (0/40)
Stenting of iliac artery (not subject of current study)	0% (0/40)
Impotence	42.5% (17/40)
Buttock claudication	0% (0/40)
Uncorrectable coagulopathy	0% (0/40)
Endarterectomy	0% (0/40)
Hypertension	77.5% (31/40)
Pulmonary	
Chronic obstructive pulmonary disease (COPD)	25.0% (10/40)
Home oxygen	2.5% (1/40)
Renal	
Chronic renal failure	2.5% (1/40)
Dialysis	0% (0/40)
Renal insufficiency	10.0% (4/40)
Endocrine	
Diabetes	27.5% (11/40)
Infectious disease	
Systemic infection	10.0% (4/40)
Gastrointestinal	
Gastrointestinal disease	30.0% (12/40)
Hepatobiliary	
Liver disease	15.0% (6/40)
Neoplasms	
Cancer	15.0% (6/40)
Neurologic	
Stroke	12.5% (5/40)
Allergies	47.5% (19/40)
Smoking	
Current	27.5% (11/40)
Quit	47.5% (19/40)
Never	25.0% (10/40)

Baseline Anatomical Measurements

Patients underwent pre-procedure imaging to evaluate iliac morphology (Table 9). Measurements provided are reported on the same side as the intended side for treatment (i.e., left or right) with ZBIS.

Table 9. Pre-procedure anatomical measurements in the iliac arteries

Measurement	Mean ± SD (N, Range)
	Site
At intended distal fixation site (mm)	
EIA outer diameter	10.2 ± 1.4 (40, 8.0 – 13.0)
EIA fixation length	44.7 ± 29.5 (40, 20.0 – 134.0)
IIA inner diameter	8.0 ± 0.9 (40, 6.9 – 10.0)
IIA outer diameter	8.8 ± 0.9 (40, 7.0 – 10.0)
IIA fixation length	20.5 ± 7.1 (40, 10.0 – 40.0)
Iliac artery diameters	
CIA maximum diameter (outer-wall)	35.9 ± 10.1 (40, 20.0 – 62.9)
EIA minimum diameter (access) (inner-wall)	10.6 ± 9.4 (40, 7.1 – 68.0)
EIA maximum diameter (outer-wall)	10.4 ± 1.8 (40, 7.3 – 15.0)
CIA lumen diameter just proximal to IIA	21.4 ± 6.4 (40, 13.9 – 42.6)
IIA maximum diameter (outer-wall)	9.7 ± 3.0 (40, 6.5 – 25.0)
IIA lumen diameter of ostia	8.1 ± 2.6 (40, 5.0 – 20.0)
Iliac artery lengths (mm)	
CIA length from aortic bifurcation to iliac bifurcation	70.9 ± 14.8 (40, 50.0 – 121.0)
IIA length from ostia to anterior-posterior division	33.8 ± 19.0 (40, 19.0 – 140.0)
Iliac artery angles and location (degrees)	
Angle of IIA to EIA	55.4 ± 31.5 (39, 15.0 – 153.0)
Angle of right CIA to left CIA	54.4 ± 22.2 (39, 0 – 125.0)
Circumferential location of IIA (degrees)[a]	150.8 ± 50.2 (39.0, 23.0 – 270.0)

Note: CIA = common iliac artery; EIA = external iliac artery; IIA = internal iliac artery.

[a] Circumferential location of the IIA is measured from 0 to 360 degrees with 0 degrees being anterior, 90 degrees being left, 180 degrees being posterior, and 270 degrees being right.

The extent of calcification was defined as either none (lack of calcification), mild (less than 40% circumferential calcification), moderate (between 40% and 70% circumferential calcification), or severe (greater than 70% circumferential calcification). The extent of occlusive disease was defined as either none (lack of occlusive disease), mild (some disease, focal with less than 30% narrowing), moderate (between 30-50% narrowing), or severe (greater than 50% narrowing). Tortuosity was defined as either none (no tortuosity), mild (minimal tortuosity with less than one turn involving either external or common iliac artery), moderate (single turn involving either external or common iliac artery), or severe (compound turns involving external and common iliac arteries). Per the site assessment, most patients had none or mild calcification and occlusive disease in the iliac arteries. Mild or moderate iliac tortuosity was reported in 75% of patients.

D. Procedural Information

Table 10 reports anesthesia and access methods used to support device placement. Most procedures were performed under general anesthesia (90.0%, 36/40). Vascular access was obtained primarily via percutaneous (52.5%, 21/40) or femoral artery cutdown (45.0%, 18/40) access technique during insertion of ZBIS.

Table 10. Primary anesthesia type and access method

Characteristic	Percent Patients (number/total number)
Anesthesia Method	
Local	5.0% (2/40)
Regional	5.0% (2/40)[a]
General	90.0% (36/40)
Access Method	
Percutaneous	52.5% (21/40)
Cutdown	45.0% (18/40)
Cutdown/Percutaneous	2.5% (1/40)
Iliac conduit	0% (0/40)

[a] One patient received both regional and monitored anesthesia care.

Procedural measures are detailed in Table 11. The average procedure time was 210.5 ± 53.4 minutes with an average fluoroscopy time of 40.1 ± 15.7 minutes. The average total contrast volume used was 128.2 ± 63.5 cc with an average concentration of 310.0 ± 40.8 mgI/mL. Most patients (60%, 24/40) received non-ionic contrast agents. The average estimated blood loss was 275.6 ± 215.5 cc (maximum blood loss was 800 cc).

Table 11. Procedural times, monitoring, and blood loss

Parameter	Mean ± SD (n, range) or Percent Patients (number/total number)
Procedure (min)	210.5 ± 53.4 (37, 123 – 331)
Fluoroscopy (min)	40.1 ± 15.7 (39, 12 – 93)
Total amount of contrast used (cc)	128.2 ± 63.5 (39, 35 – 328)
Concentration of contrast (mgI/mL)	310.0 ± 40.8 (40, 100 – 370)
Type of contrast agent[a]	
Ionic	25.0% (10/40)
Non-ionic	60.0% (24/40)
Iso-osmolar	17.5% (7/40)
Non-iso-osmolar	12.5% (5/40)
Estimated blood loss (cc)	275.6 ± 215.5 (40, 0 – 800)
Blood bank products received	
PRBC	5.0% (2/40)
FFP	0% (0/40)
Platelets	0% (0/40)
Cryoprecipitate	0% (0/40)
Cell saver	5.0% (2/40)
Amount of blood products received (cc)	
PRBC	350.0 ± 0 (2, 350 – 350)
FFP	N/A
Platelets	N/A
Cryoprecipitate	N/A
Cell saver	275.0 ± 14.1 (2, 265 – 285)

[a] Patients can receive multiple types of contrast agent and may appear on more than one row.

Devices Placed during Index Procedure

Table 12 reports the number and size of ZBIS devices placed at the index procedure. In total, 40 ZBIS devices were placed in 40 study patients. The Reference Part Number (RPN) for the ZBIS is presented in the following format according to the lengths and diameter of the ZBIS (mm): ZBIS-XX-YY-ZZ, where XX is distal diameter, YY is the Common Iliac Segment

Length (length from the proximal graft edge to the tip of the sidebranch), and ZZ is the External Iliac Segment Length (length from the tip of the sidebranch to distal edge of the graft). All available ZBIS RPNs were used in the study with the most common being ZBIS-12-61-58 (27.5%, 11/40) and ZBIS-12-45-58 (22.5%, 9/40).

Table 12. ZBIS sizes used in the PRESERVE clinical study

Distal Diameter (mm)	**10**	**12**	**10**	**12**	**10**	**12**	**10**	**12**	**Total # ZBIS**
Common Iliac Segment Length (CISL) (mm)	**45**	**45**	**45**	**45**	**61**	**61**	**61**	**61**	
External Iliac Segment Length (EISL) (mm)	**41**	**41**	**58**	**58**	**41**	**41**	**58**	**58**	
Total	2	5	2	9	2	4	5	11	40

The number and size of iCAST stents implanted during the study procedures are shown in Table 13. In total, 47 iCAST stents were implanted in the 40 study patients. The most common iCAST stent sizes implanted were the 9 x 59 mm (29.8%, 14/47) and 9 x 38 mm (27.7%, 13/47) stents. Six patients received more than one iCAST stent deployed within the sidebranch of the ZBIS. Specifically, five patients received two iCAST stents and one patient received three iCAST stents. The use of multiple iCAST stents was to obtain either maximal seal distally within the internal iliac artery or to ensure optimal overlap within the ZBIS sidebranch.

Table 13. iCast covered stent sizes used in the PRESERVE clinical study

Diameter (mm)	**Length (mm)**		**Total**
	38	**59**	
8	7	5	12
9	13	14	27
10	8	N/A[a]	8
Total	28	19	47

[a] 10 x 59 mm iCAST stents were not available in the United States during this study.

ZBIS is used in combination with the Zenith Flex AAA endovascular graft and Zenith iliac leg grafts (ZSLE). The number and size of these additional endovascular components used in the pivotal study are shown in Table 14. In total, 40 Zenith Flex AAA Endovascular Grafts were implanted in the 40 patients. A ZSLE is deployed into the short (contralateral) leg of the Zenith Flex AAA Endovascular Graft, connecting the lumen of the main body graft to the ZBIS stent. An additional ZSLE is deployed into the long (ipsilateral) leg of the Zenith Flex AAA Endovascular Graft. More than one ZSLE may be deployed on either side according to physician discretion. In total, 44 ZSLE stents were implanted within the contralateral leg of the Zenith Flex AAA Endovascular Graft with 4 patients receiving more than one ZSLE stent (same side as ZBIS). In total, 41 ZSLE stents were implanted within the ipsilateral leg of the Zenith Flex AAA Endovascular Graft with 2 patients receiving more than one ZSLE stent (opposite side as ZBIS).

Table 14. Zenith Flex AAA Endovascular Graft and ZSLE stents used

	Same side as ZBIS		Opposite side as ZBIS	
Zenith Flex AAA Endovascular Graft	**ZSLE**	**Additional ZSLE**	**ZSLE**	**Additional ZSLE**
40	40	4	39[a]	2

[a] One patient did not receive a ZSLE on the opposite side as ZBIS.

Clinical utility measures are reported in Table 15. The average ICU stay was 17.1 ± 32.7 hours and the average length of time to hospital discharge was 2.0 ± 2.4 days.

Table 15. Clinical utility measures

Clinical utility	Mean ± SD (range), Total
Duration of ICU stay (hours)	17.1 ± 32.7 (38, 0 – 144)
Days to first ambulation	1.0 ± 0.8 (40, 0 – 5)
Days to resumption of oral fluid intake	0.4 ± 0.6 (40, 0 – 3)
Days to resumption of regular diet	0.8 ± 0.8 (40, 0 – 4)
Days to first bowel movement	2.1 ± 1.8 (30, 0 – 8)
Days to discharge	2.0 ± 2.4 (40, 0 – 14)

E. Safety and Effectiveness Results

1. Safety and Effectiveness Results

The primary safety and effectiveness endpoint was prospectively defined as 6-month freedom from patency-related intervention, which is defined as a secondary intervention to treat a > 60% stenosis of the internal iliac artery (as identified through computed tomography (CT) scan, angiography, or duplex ultrasound and confirmed by core laboratory) associated with clinical symptoms. Of note, this endpoint definition not only includes patients with internal iliac artery stenosis following successful placement of the ZBIS and covered bridging stent, but also any cases of technical failure resulting in occlusion of the internal iliac artery during the initial implant procedure that require secondary intervention for associated clinical symptoms. The results for 6-month freedom from patency-related intervention are presented in Table 16.

The success rate for the primary safety and effectiveness endpoint was 100% (39/39) of patients, and the 2.5th percentile of the Bayesian posterior distribution was 91.2%, surpassing the performance goal of 55%. Based on these results, the primary endpoint for the study was met.

Endpoint data were available for 39 patients due to the death of one patient prior to the 6-month follow-up visit; based on an intent-to-treat analysis, including this patient either as a success (40/40) or as a failure (39/40), the observed rate for the primary endpoint also met the established performance goal (posterior probability < 0.01).

Table 16. 6-month freedom from patency-related intervention

6-month freedom from patency-related reintervention	Performance goal	Lower bound[a]	Posterior probability	Performance goal met
100% (39/39)	55%	91.2%	< 0.01	Yes

[a] The lower bound, per the protocol, is the 2.5th percentile of the Bayesian posterior distribution

2. Secondary Safety Results

The secondary safety endpoint for the study was 30-day freedom from morbidity (i.e., the morbidity index defined in Section X.A.3 above).

The results for 30-day freedom from morbidity are presented in Table 17. Safety data through 30 days were available for all 40 patients. The success rate for the secondary safety endpoint was 85% (34/40) of patients, and the 2.5th percentile of the Bayesian posterior distribution was 70.8%, surpassing the performance goal of 46%. Based on these results, the secondary safety endpoint for the study was met.

Six patients experienced morbid events within 30 days of the procedure: distal embolization resulting in tissue loss or requiring reintervention (n = 1), inotropic support (n = 1), pneumonia requiring antibiotics (n = 1), paralytic ileus > 4 days (n = 1), impotence (n=1), and limb thrombosis on the same side as the ZBIS (n = 1).

Table 17. 30-day freedom from morbidity

30-day freedom from morbidity	Performance goal	Lower Bound[a]	Posterior probability	Performance goal met
85% (34/40)	46%	70.8%	< 0.01	Yes

[a] The lower bound, per the protocol, is the 2.5th percentile of the Bayesian posterior distribution.

3. Additional Safety Outcomes

Death, Rupture, and Conversion

Kaplan-Meier estimates for freedom from death, rupture, and conversion to open surgical repair are reported in Table 18. Among the 40 study patients, there was one death through 1 year; the freedom from all-cause mortality was 97.5%. In total, there were four deaths during the study; the 5-year freedom from all-cause mortality was 88.5%. There were no aneurysm-related deaths in the study. Likewise, there were no ruptures or conversions to open surgical repair during the study.

Table 18. Kaplan-Meier estimates (freedom from death, rupture, and conversion)

Serious Adverse Event	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
All-cause mortality	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	1[a]	1	1	1	2[a,b]	4[a-d]
	Cumulative censored	0	0	2	2	4	5	18
	Kaplan-Meier estimate	100%	97.5%	97.5%	97.5%	97.5%	94.6%	88.5%
	Standard error	0%	2.5%	2.5%	2.5%	2.5%	3.8%	5.7%
Aneurysm-related mortality	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	0
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%	0%
Rupture	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	0
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%	0%

Serious Adverse Event	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Conversion	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	0
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%	0%

[a] Respiratory failure from CHF on POD 167; CEC adjudication was not related; related to pre-existing condition
[b] Malignant neoplasm of bladder with metastasis to liver and spine on POD 1383; CEC adjudication was not related; related to pre-existing condition
[c] Multi-factorial acute hypoxic respiratory failure on POD 1570; CEC adjudication was not related; related to fall, rib fractures, respiratory failure
[d] Unknown cause of death on POD 1723; CEC was unable to adjudicate

Adverse Effects that Occurred in the PMA Clinical Study

A total of 29 patients (72.5%) had a total of 141 adverse events. Table 19 reports Kaplan-Meier estimates for all adverse events according to category.

In particular, several types of vascular adverse events were reported during study follow-up.

- Additional aneurysms (5 events) were reported in four patients. Three of these aneurysms occurred in the iliac arteries on the side opposite the ZBIS and were all successfully treated with either stent placement (n=2) or bypass (n=1). The remaining two aneurysms occurred in the thoracic aorta, one requiring surgical replacement of the aortic root and ascending aorta and the other occurring in the ascending aorta and was not treated.
- Thrombosis events were reported in three patients, two of which had thrombosis of the external iliac segment of the ZBIS resulting in an occlusion. Both were treated with a secondary intervention involving thrombectomy and stent placement and were reported to have successfully restored patency. The third patient had thrombosis and occlusion of the iCAST stent in the IIA, on which no treatment was performed.
- Embolization with ischemia or infarction of the left gluteal area was reported in one patient on same day as the index procedure. Four surgical treatments were performed involving surgical exploration, drainage, and debridement of the left gluteal area and left buttock after which the event was considered to have resolved.
- Vascular injury was reported in 2 patients. One vascular injury was reported to be a stenosis of the external iliac artery at the distal edge of the ZBIS resulting in a secondary intervention which included balloon angioplasty and stent placement. The second vascular injury was reported to be an occlusion of the IIA (same side as ZBIS) that did not require treatment.

Table 19. Kaplan-Meier estimates (freedom from morbidity)

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Access site/incision	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	0
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%	0%
Cardiovascular	Number at risk	39	38	36	33	30	28	16
	Cumulative events	1	1	1	4	5	5	5
	Cumulative censored	0	1	3	3	5	7	19
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	89.4%	86.5%	86.5%	86.5%
	Standard error	2.5%	2.5%	2.5%	5.1%	5.8%	5.8%	5.8%

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Cardiac arrhythmia	Number at risk	39	38	36	35	32	30	17
	Cumulative events	1	1	1	2	3	3	3
	Cumulative censored	0	1	3	3	5	7	20
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	94.8%	91.9%	91.9%	91.9%
	Standard error	2.5%	2.5%	2.5%	3.7%	4.6%	4.6%	4.6%
Congestive heart failure (CHF)	Number at risk	40	39	37	36	33	31	17
	Cumulative events	0	0	0	1	2	2	2
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	97.3%	94.4%	94.4%	94.4%
	Standard error	0%	0%	0%	2.7%	3.9%	3.9%	3.9%
Myocardial Infarction (MI)	Number at risk	40	39	37	36	34	32	17
	Cumulative events	0	0	0	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	0%	2.7%	2.7%	2.7%	2.7%
Cerebrovascular/ neurologic	Number at risk	40	39	36	36	33	31	17
	Cumulative events	0	0	2	2	3	3	3
	Cumulative censored	0	1	2	2	4	6	20
	Kaplan-Meier estimate	100%	100%	94.8%	94.8%	92.0%	92.0%	92.0%
	Standard error	0%	0%	3.6%	3.6%	4.5%	4.5%	4.5%
Transient ischemic attack	Number at risk	40	39	36	36	34	32	18
	Cumulative events	0	0	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	97.3%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	2.7%	2.7%	2.7%	2.7%	2.7%
Stroke	Number at risk	40	39	37	37	34	32	17
	Cumulative events	0	0	1	1	2	2	2
	Cumulative censored	0	1	2	2	4	6	21
	Kaplan-Meier estimate	100%	100%	97.4%	97.4%	94.7%	94.7%	94.7%
	Standard error	0%	0%	2.5%	2.5%	3.8%	3.8%	3.8%
Gastrointestinal	Number at risk	39	38	36	36	34	32	18
	Cumulative events	1	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Bleeding requiring intervention	Number at risk	40	39	37	37	34	32	18
	Cumulative events	0	0	0	0	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	100%	97.2%	97.2%	97.2%
	Standard error	0%	0%	0%	0%	2.7%	2.7%	2.7%
Infection	Number at risk	40	39	37	37	34	32	18
	Cumulative events	0	0	0	0	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	100%	97.2%	97.2%	97.2%
	Standard error	0%	0%	0%	0%	2.7%	2.7%	2.7%
Ileus	Number at risk	39	38	36	36	34	32	18
	Cumulative events	1	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Hepatic	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	0
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%	0%
Pulmonary	Number at risk	38	36	34	33	27	25	13
	Cumulative events	2	3	3	4	8	8	8
	Cumulative censored	0	1	3	3	5	7	19
	Kaplan-Meier estimate	95.0%	92.5%	92.5%	89.8%	78.5%	78.5%	78.5%
	Standard error	3.4%	4.2%	4.2%	5.0%	7.0%	7.0%	7.0%
Chronic obstructive pulmonary disease (COPD)	Number at risk	40	39	37	37	32	30	15
	Cumulative events	0	0	0	0	3	3	4
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	100%	91.6%	91.6%	88.3%
	Standard error	0%	0%	0%	0%	4.7%	4.7%	5.8%
Pneumothorax	Number at risk	40	38	36	36	34	32	17
	Cumulative events	0	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	0%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Pulmonary embolism	Number at risk	39	38	36	36	33	31	17
	Cumulative events	1	1	1	1	2	2	2
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	94.6%	94.6%	94.6%
	Standard error	2.5%	2.5%	2.5%	2.5%	3.8%	3.8%	3.8%
Pneumonia	Number at risk	39	38	36	35	32	30	16
	Cumulative events	1	1	1	2	3	3	3
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	94.8%	92.0%	92.0%	92.0%
	Standard error	2.5%	2.5%	2.5%	3.7%	4.5%	4.5%	4.5%
Renal/urologic	Number at risk	39	37	35	33	30	30	16
	Cumulative events	1	2	2	4	5	5	6
	Cumulative censored	0	1	3	3	5	5	18
	Kaplan-Meier estimate	97.5%	95.0%	95.0%	89.6%	86.8%	86.8%	83.9%
	Standard error	2.5%	3.4%	3.4%	5.0%	5.7%	5.7%	6.3%
Renal failure requiring dialysis	Number at risk	40	39	37	37	35	33	18
	Cumulative events	0	0	0	0	0	0	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%	97.0%
	Standard error	0%	0%	0%	0%	0%	0%	3.0%
Urinary Tract Infection (UTI)	Number at risk	39	37	35	34	32	31	16
	Cumulative events	1	2	2	3	3	4	4
	Cumulative censored	0	1	3	3	5	5	20
	Kaplan-Meier estimate	97.5%	95.0%	95.0%	92.3%	92.3%	89.4%	89.4%
	Standard error	2.5%	3.4%	3.4%	4.4%	4.4%	5.2%	5.2%
Serum creatinine rise > 30% above baseline resulting in a persistent value > 2 mg/dl	Number at risk	40	39	37	36	33	31	17
	Cumulative events	0	0	0	1	2	2	2
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	100%	100%	100%	97.3%	94.5%	94.5%	94.5%
	Standard error	0%	0%	0%	2.7%	3.8%	3.8%	3.8%
Vascular	Number at risk	36	34	32	30	27	25	13
	Cumulative events	4	5	5	7	8	8	9
	Cumulative censored	0	1	3	3	5	7	18
	Kaplan-Meier estimate	90.0%	87.5%	87.5%	82.0%	79.1%	79.1%	75.9%
	Standard error	4.7%	5.2%	5.2%	6.3%	7.0%	7.0%	7.6%

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Aneurysm	Number at risk	40	39	37	36	32	30	17
	Cumulative events	0	0	0	1	3	3	4
	Cumulative censored	0	1	3	3	5	7	19
	Kaplan-Meier estimate	100%	100%	100%	97.3%	91.6%	91.6%	88.5%
	Standard error	0%	0%	0%	2.7%	4.7%	4.7%	5.6%
Thrombosis	Number at risk	39	37	35	34	32	30	16
	Cumulative events	1	2	2	3	3	3	3
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	95.0%	95.0%	92.3%	92.3%	92.3%	92.3%
	Standard error	2.5%	3.4%	3.4%	4.4%	4.4%	4.4%	4.4%
Embolization with ischemia or infarction	Number at risk	39	38	36	36	34	32	18
	Cumulative events	1	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Buttock claudication (total)	Number at risk	40	39	37	36	34	32	17
	Cumulative events	0	0	0	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	0%	2.7%	2.7%	2.7%	2.7%
Same side as investigational devices	Number at risk	40	39	37	36	34	32	17
	Cumulative events	0	0	0	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	0%	2.7%	2.7%	2.7%	2.7%
Opposite side from investigational devices	Number at risk	40	39	37	36	34	32	17
	Cumulative events	0	0	0	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	0%	2.7%	2.7%	2.7%	2.7%
Vascular injury	Number at risk	40	39	36	36	34	32	16
	Cumulative events	0	0	1	1	1	1	2
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	97.3%	97.3%	97.3%	97.3%	94.3%
	Standard error	0%	0%	2.7%	2.7%	2.7%	2.7%	4.1%

Category	Parameter	30 Days	180 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Leg claudication	Number at risk	39	38	36	36	34	32	17
	Cumulative events	1	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Deep vein thrombosis (DVT)	Number at risk	40	39	37	36	34	32	17
	Cumulative events	0	0	0	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	100%	100%	100%	97.3%	97.3%	97.3%	97.3%
	Standard error	0%	0%	0%	2.7%	2.7%	2.7%	2.7%
Lower extremity ischemia	Number at risk	39	38	36	36	34	32	17
	Cumulative events	1	1	1	1	1	1	1
	Cumulative censored	0	1	3	3	5	7	22
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%	97.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%
Miscellaneous	Number at risk	32	26	19	15	13	11	4
	Cumulative events	8	13	18	22	23	24	25
	Cumulative censored	0	1	3	3	4	5	11
	Kaplan-Meier estimate	80.0%	67.3%	53.8%	42.5%	39.4%	36.4%	32.8%
	Standard error	6.0%	7.0%	7.6%	7.2%	7.2%	7.0%	7.2%
Impotence	Number at risk	39	37	34	33	31	29	15
	Cumulative events	1	2	3	4	4	4	5
	Cumulative censored	0	1	3	3	5	7	20
	Kaplan-Meier estimate	97.5%	95.0%	92.4%	89.7%	89.7%	89.7%	86.4%
	Standard error	2.5%	3.4%	4.2%	5.0%	5.0%	5.0%	6.3%
Sepsis	Number at risk	39	38	36	36	33	31	15
	Cumulative events	1	1	1	1	2	3	4
	Cumulative censored	0	1	3	3	5	6	21
	Kaplan-Meier estimate	97.5%	97.5%	97.5%	97.5%	94.7%	91.8%	88.5%
	Standard error	2.5%	2.5%	2.5%	2.5%	3.7%	4.7%	5.8%
Other[a]	Number at risk	33	27	20	16	14	12	5
	Cumulative events	7	12	17	21	22	23	24
	Cumulative censored	0	1	3	3	4	5	11
	Kaplan-Meier estimate	82.5%	69.8%	56.3%	45.0%	42.0%	39.0%	35.5%
	Standard error	5.7%	6.9%	7.6%	7.3%	7.3%	7.2%	7.4%

[a] Other adverse events included multiple conditions such as cardiovascular issues (e.g., angina, elevated troponin, coronary artery stenosis), chronic musculoskeletal problems (e.g., osteoarthritis, back pain), repeated occurrences of infection (e.g., bacteremia, cellulitis, and abscesses), systemic issues (e.g., hypotension, adrenal insufficiency), and cancer and oncological disorders (e.g., prostate cancer, metastatic thyroid cancer).

4. Additional Effectiveness Results

6-month branch vessel patency

The secondary effectiveness endpoint for the study was 6-month branch vessel (i.e., internal iliac artery) patency (reported for descriptive purposes only), and the results are presented in Table 20.

The success rate for the secondary effectiveness endpoint was 100% (37/37) of patients based on available imaging analyzed by the core laboratory at 6 months.

Table 20. Results for 6-month branch vessel patency based on core lab analysis

6-month branch vessel patency	95% Confidence interval
100% (37/37)[a]	88.8%, 100%

[a] Three patients who did not complete 6-month CT imaging were excluded from the analysis of branch vessel patency at 6 months.

Technical success

Technical success was defined as the ability to deliver and deploy the ZBIS and covered bridging stent in the desired location; graft patency and internal iliac artery patency following deployment, as evidenced by intraoperative angiography; and successful removal of the delivery system. Overall, all 40 patients were reported to have had successful deployment of the ZBIS System (i.e., AAA graft, iliac leg grafts, ZBIS, and iCAST stent). This resulted in a technical success rate of 100% (40/40) for the ZBIS and iCAST stent as presented in Table 21.

Table 21. Technical Success

Success Measure	Percent Patients (n/N)
Technical success	100% (40/40)

Procedural Success

Procedural success, which was defined as technical success with no Type I, Type III, or Type IV endoleaks at 30 days; no procedure-related major complications through 30 days; freedom from patency-related intervention through 30 days; and endovascular graft patency through 30 days, as evidenced by CT scan, angiography, or duplex ultrasound in those patients experiencing renal failure and unable to undergo contrast-enhanced CT scan. Overall, the rate of procedural success was 87.5% (35/40) is reported in Table 22. Of the five patients who failed to meet procedural success, three were due to major complications (impotence, ileus, and lower extremity ischemia) and two were due to occlusion of the ZBIS.

Table 22. Procedural Success

Success Measure	Percent Patients (n/N)
Procedural success	87.5% (35/40)

Changes in Aneurysm Size

To characterize changes in the treated common iliac aneurysm size, aneurysm shrinkage was defined as a decrease in aneurysm maximum diameter of > 5 mm from the first post-procedure measurement (i.e., 1-month exam). Likewise, aneurysm growth was defined as an increase in maximum aneurysm diameter of > 5 mm from the first post-procedure measurement. Lastly, no change was defined as an increase or decrease in maximum aneurysm diameter ≤ 5 mm as compared to the first post-procedure measurement. Changes in aneurysm size throughout study follow-up are detailed in Table 23.

Only one patient (2.5%, 1/40) experienced an increase in common iliac aneurysm size on the ZBIS side during the study. The patient had a reported increase in size of 5.5 mm as measured by the core laboratory on the 4-year CT scan. The site reported a similar growth of 7 mm on the same 4-year CT. This patient was also noted by the core laboratory to have had a distal Type I endoleak involving the iCAST stent persisting from 12-months to the 5-year imaging exam and a Type II endoleak persisting from 4-year to 5-year imaging exam; notably, the site only reported presence of a Type II endoleak. The aneurysm growth was not treated with a secondary intervention. Despite this, growth was not identified by the core laboratory at 5 years.

Table 23. Change in common iliac artery aneurysm size based on results from core laboratory analysis

Status	% Patient (number/total number)					
	6-month	12-month	2-year	3-year	4-year	5-year
Increase (> 5 mm)	0% (0/37)	0% (0/37)	0% (0/28)	0% (0/31)	3.6% (1/28)[a]	0% (0/26)
Decrease (> 5 mm)	10.8% (4/37)	16.2% (6/37)	21.4% (6/28)	29.0% (9/31)	25.0% (7/28)	26.9% (7/26)
No change (≤ 5 mm)	89.2% (33/37)	83.8% (31/37)	78.6% (22/28)	71.0% (22/31)	71.4% (20/28)	73.1% (19/26)

[a] One patient had aneurysm growth reported at 4 years, but no growth at 5 years. The patient also had an associated distal Type I endoleak involving the iCAST stent reported consistently from 12-months through 5-years and a Type II endoleak reported at 4-years and 5-years. No reintervention to treat the aneurysm growth was performed.

Endoleaks

Endoleak events by type, as assessed by the core laboratory at each follow-up exam period are reported in Table 24. In total, one patient (2.5%, 1/40) had a reported Distal Type I endoleak which was first identified on the 12-month CT exam and persisted through the 5-year CT exam. This Distal Type I endoleak was on the same side as the ZBIS and involved the iCAST stent. Of note, the site did not report a Distal Type I endoleak, but rather a Type II endoleak at 12 months through 5 years. This patient experienced growth of the CIA aneurysm at 4 years and no secondary intervention was performed for the endoleak; of note, no aneurysm growth was identified at 5-years. No Type III or Type IV endoleaks were reported in the study.

Table 24. Endoleak results from core laboratory analysis

Type	% Patient (number/total number)							
	1-month	6-month	12-month	2-year	3-year	4-year	5-year	Total
Any (new only)	22.5% (9/40)	2.7% (1/37)	5.6% (2/36)	0% (0/27)	0% (0/29)	3.4% (1/29)	0% (0/25)	N/A
Any (new and persistent)	37.5% (15/40)	32.4% (12/37)	30.6% (11/36)	33.3% (9/27)	34.5% (10/29)	34.5% (10/29)	36.0% (9/25)	19
Multiple	0% (0/40)	0% (0/37)	0% (0/36)	0% (0/27)	3.4% (1/29)	6.9% (2/29)	8.0% (2/25)	2
Proximal Type I	0% (0/40)	0% (0/37)	0% (0/36)	0% (0/27)	0% (0/29)	0% (0/29)	0% (0/25)	0
Distal Type I	0% (0/40)	0% (0/37)	2.8% (1/36)	3.7% (1/27)	3.4% (1/29)	3.4% (1/29)	4.0% (1/25)	1
Type II	35.0% (14/40)	32.4% (12/37)	27.8% (10/36)	29.6% (8/27)	31.0% (9/29)	31.0% (9/29)	36.0% (9/25)	17
Type III	0% (0/40)	0% (0/37)	0% (0/36)	0% (0/27)	0% (0/29)	0% (0/29)	0% (0/25)	0
Type IV	0% (0/40)	0% (0/37)	0% (0/36)	0% (0/27)	0% (0/29)	0% (0/29)	0% (0/25)	0
Unknown	2.5% (1/40)	0% (0/37)	0% (0/36)	0% (0/27)	3.4% (1/29)	6.9% (2/29)	4.0% (1/25)	3

Device Migration

Radiographic migration was defined as movement of a component ≥ 10 mm. Clinically significant migration was defined as movement of the stent-graft that requires surgical or endovascular intervention. There were no reported instances of radiographic migration or clinically significant migration of the ZBIS or iCAST stent during this study.

Occlusion

Occlusions reported on the same side and opposite side of the ZBIS are reported in Table 25. In total, occlusions were reported in four patients (10%; 4/40). Two patients were reported to have occlusion within the external iliac artery segment of the ZBIS; in both cases patency was restored through a secondary intervention. Additionally, two patients were reported to have occlusion within the IIA in the iCAST stent; neither patient was treated with a secondary intervention and patency was not restored. Of the two patients with IIA occlusion, one did not have any reported clinical sequalae associated with the occlusion. The other patient had a reported event of buttock claudication; however, this was reported before the occlusion of IIA and is therefore unlikely to be related.

Table 25. Occlusion based on results from core laboratory analysis

Side of Event	1-month	6-month	12-month	2-year	3-year	4-year	5-year	Total
Same side as ZBIS								
Common iliac (CIA) segment	0	0	0	0	0	0	0	0
External iliac (EIA) segment	2[a,b]	0	0	0	0	0	0	2[a,b]
Internal iliac (IIA) segment	0	0	1[c]	1[c]	0	2[c,d]	2[c,d]	2[c,d]
Opposite side as ZBIS	0	0	0	0	0	0	0	0

[a] EIA occlusion within the ZBIS; thrombectomy and stent placement performed.
[b] EIA occlusion within the ZBIS; thrombolysis and stent placement performed.
[c] IIA occlusion within the iCAST stent. No secondary intervention was performed, as the patient was reported to be asymptomatic. Of note, because the 3-year CT scan was not performed, the occlusion could not be evaluated. However, the IIA occlusion persisted at 4 and 5 years.
[d] IIA occlusion within the iCAST stent and sidebranch of the ZBIS. No secondary intervention has been performed. IIA occlusion persisted at 5 years.

Device Integrity

There were no reported device integrity issues for the ZBIS or iCAST stent during the study (e.g., fracture, separation).

Secondary Interventions

A total of nine patients underwent 15 secondary interventions. Secondary interventions have been separated into those on the same side as the ZBIS, those on the side opposite the ZBIS, and those that occurred within the aorta. The indications and types of secondary intervention are reported in Tables 26 and 27, respectively. Six secondary interventions occurred on the same side as the ZBIS, eight secondary interventions occurred on the side opposite the ZBIS, and one secondary intervention occurred within the aorta. Four of the secondary interventions (all reported for one patient) were attributed to adverse events associated with the embolization of the IIA on the side opposite the investigational devices (ZBIS and iCAST). The six secondary interventions which occurred on the same side of the ZBIS occurred in four total patients. These interventions most commonly involved placement of an additional stent for the treatment of an occlusion, thrombosis, or endoleak.

Table 26. Indications for secondary intervention (as reported by site)

Reason	0-30 Days	31-180 Days	181-365 Days	366-730 Days	731-1095 Days	1096-1460 Days	1461-1825 Days	Total # SIs
Clinical								
Symptoms	2[a,b]	3[a]	0	0	0	0	0	5
Imaging results								
Aneurysm rupture	0	0	0	0	0	0	0	0
Device stenosis	0	0	0	1[d]	0	0	0	1
Device migration	0	0	0	0	0	0	0	0
Device separation	0	0	0	0	0	0	0	0
Occlusion	1[b]	1[c]	0	0	0	0	0	2
Device kink	0	0	1[d]	1[e]	0	0	0	2
Infection	0	1[a]	0	0	0	0	0	1
Endoleak								
Type I proximal	0	0	0	0	0	0	0	0
Type I distal	0	0	0	0	0	0	0	0
Type II	0	0	0	0	0	1[g]	0	1
Type III	0	0	0	0	0	0	0	0
Type IV	0	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0	0
Other imaging results	0	0	0	2[b,e]	0	3[c,f,h]	1[i]	6
Other	0	1[a]	0	0	0	0	0	1
							Total # SIs	15[j]

Note: CIA = common iliac artery; EIA = external iliac artery; IIA = internal iliac artery.

[a] Clinical signs and symptoms (opposite side of ZBIS; POD 1, 93, 94, 112); infection (opposite side of ZBIS; POD 93); and other: extensive soft tissue air dissecting throughout the left gluteus minimus, medius, and maximus muscles with incomplete visualization of open wound of left buttock distribution (opposite side of ZBIS; POD 93).

[b] Clinical signs and symptoms and occlusion of external iliac (same side as ZBIS; POD 12); and other imaging results: stenosis of the native iliac artery at the distal edge of the ZBIS limb (same side as ZBIS; POD 390).

[c] Occlusion of external iliac artery (same side as ZBIS; POD 60); and other imaging results: increased size of common iliac artery aneurysm (opposite side of ZBIS; POD 1222).

[d] Device kink (same side as ZBIS; POD 251); and device stenosis (same side as ZBIS; POD 402).

[e] Device kink (opposite side of ZBIS) and other imaging results: loss of IIA seal (same side as ZBIS) (POD 380).

[f] Other imaging results: enlargement of CIA aneurysm (opposite side as ZBIS; POD 1173)

[g] Persistent endoleak – Type II endoleak (aorta; POD 1263).

[h] Other imaging results: iliac artery aneurysm (opposite side ZBIS). It was also noted presence of bilateral renal artery stenoses (POD 1246).

[i] Other imaging results: IIA aneurysm (opposite side of ZBIS; POD 1519).

[j] Out of the 9 patients with secondary interventions, multiple indications could have been reported. As a result, of the 15 secondary interventions, 19 indications were reported.

Table 27. Type of secondary intervention

Type	0-30 Days	31-180 Days	181-365 Days	366-730 Days	731-1095 Days	1096-1460 Days	1461-1825 Days	Total # SIs
Percutaneous								
Thrombolysis	0	1[c]	0	0	0	0	0	**1**
Thrombectomy	0	0	0	0	0	0	0	**0**
Balloon angioplasty	0	0	0	1[b]	0	0	1[i]	**2**
Coil embolization	0	0	0	0	0	1[f]	0	**1**
Stent placed	0	1[c]	1[d]	3[b,d,e]	0	1[h]	1[i]	**7**
Ancillary component placed:								
Iliac leg extension	0	0	0	1[e]	0	0	0	**1**
AAA main body extension	0	0	0	0	0	0	0	**0**
iCAST stent	0	0	0	1[e]	0	0	0	**1**
Other	0	0	0	1[e]	0	1[f]	0	**2**
Other percutaneous	0	0	0	1[d]	0	2[f,g]	0	**3**
Surgical								
Conversion to open repair	0	0	0	0	0	0	0	**0**
Surgical bypass procedure	0	0	0	0	0	1[c]	0	**1**
Other surgical	2[a,b]	3[a]	0	0	0	0	0	**5**
Other	0	0	1[d]	0	0	1[c]	0	**2**
							Total #SIs	**15[j]**

Note: CIA = common iliac artery; EIA = external iliac artery; IIA = internal iliac artery.

[a] Other surgical: gluteal exploration (opposite side of ZBIS; POD 1); other surgical: incision and drainage of buttock and sacrum with extensive gluteus muscle excision or debridement (opposite side of ZBIS; POD 93); other surgical: debridement of buttock and placement of buttock wound vacuum dressing (opposite side of ZBIS; POD 94); other surgical: debridement including skin and subcutaneous tissue of gluteal wound and complex closure of gluteal wound (opposite side of ZBIS; POD 112).

[b] Other surgical: femoral exposure/thrombectomy, placement of iCAST stent in EIA (same side as ZBIS; POD 12); percutaneous: balloon angioplasty and stent placement in EIA (same side as ZBIS; POD 390).

[c] Percutaneous: thrombolysis and stent placement in EIA (same side as ZBIS; POD 60); surgical: EIA to IIA bypass and other: stent placement into right CIA to EIA (opposite side of ZBIS; POD 1222).

[d] Percutaneous; stent placement and other percutaneous: deployment of stent into iliac artery (same side as ZBIS; POD 251); percutaneous: stent placement and other percutaneous in IIA (same side as ZBIS; POD 402).

[e] Percutaneous: stent placement in IIA (same side as ZBIS), ancillary components placed (iliac leg extension, iCAST stent, other stent) in CIA (opposite side as ZBIS) (POD 380).

[f] Percutaneous: ancillary components placed (other) in CIA and EIA, percutaneous other (coil embolization) in IIA (opposite side of ZBIS; POD 1173).

[g] Other percutaneous: N-butyl-2-cyanoacrylate (NBCA) embolization (aorta; POD 1263).

[h] Percutaneous: stent placed in EIA and right renal artery (opposite side of ZBIS; POD 1246).

[i] Percutaneous: balloon angioplasty and stent placement in IIA (opposite side of ZBIS; POD 1519).

[j] Out of the 9 patients with secondary interventions, multiple types could have been reported. As a result, of the 15 secondary interventions, 26 types were reported.

Subgroup Analyses

Only two female patients were enrolled, likely due to the rarity of iliac artery aneurysms in females and anatomical constraints like smaller iliac arteries that complicate endovascular treatment. No analyses were conducted for sex-specific outcomes. Similarly, due to the small sample size and the inability to draw conclusions, no analyses were performed on subgroups based on age, race, or ethnicity.

5. Pediatric Extrapolation

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

XI. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 101 principal investigators, 0 of whom none were full-time or part-time employees of the sponsor and 16 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c), and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 16
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. Summary of Supplemental Clinical Information

PRESERVE II Continued Access Cohort (Through 5 Years)

1. Summary of supplemental clinical information – continued access
   Upon completing enrollment in the pivotal study, the Agency approved a Continued Access Study. This allowed PRESERVE II investigators to treat more patients with ZBIS and iCast, adhering to the same criteria, follow-up schedule, definitions, and data collection as the pivotal study. A total of 30 patients were treated with ZBIS and iCast between 19 October 2015 and 31 January 2019 at 14 clinical sites, with follow-up through five years complete.

2. Demographics and patient characteristics

   Patients in the continued access study had an average age of 69.9 ± 8.0 years and were predominately male (96.7%, 29/30). Patients commonly presented with comorbidities including hypertension (76.7%, 23/30) and allergies (36.7%, 11/30), which aligned with the pivotal study patients. Table 28 reports patient follow-up availability through five years.

Table 28. Follow-up data availability - Continued Access Cohort (Through 5 Years)

Visit	Eligible for Follow-up	Percent of Data Available		Adequate Imaging for Core Laboratory to Assess Parameter					Events Occurring Before Next Interval			
		Clinical Exam	CT	Size Increase	Endoleak	Patency	Migration	Device Integrity	Death	Conversion	Lost to Follow-up (LTF)	Withdrawal
Procedure	30	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0	0	0	0
Pre-discharge	30	100% (30/30)	N/A	N/A	N/A	N/A	N/A	N/A	0	0	0	0
1-month	30	96.7% (29/30)	100% (30/30)	N/A	100% (30/30)	100% (30/30)	N/A	100% (30/30)	0	0	0	0
6-month	30	93.3% (28/30)	90.0% (27/30)	93.3% (28/30)	93.3% (28/30)	93.3% (28/30)	90.0% (27/30)	90.0% (27/30)	0	0	1	0
12-month	29	93.1% (27/29)	93.1% (27/29)	93.1% (27/29)	89.7% (26/29)	93.1% (27/29)	93.1% (27/29)	93.1% (27/29)	1	0	0	1
2-year	27	92.6% (25/27)	96.3% (26/27)	96.3% (26/27)	92.6% (25/27)	92.6% (25/27)	96.3% (26/27)	96.3% (26/27)	0	0	0	2
3-year	25	92.0% (23/25)	96.0% (24/25)	96.0% (24/25)	88.0% (22/25)	96.0% (24/25)	96.0% (24/25)	96.0% (24/25)	0	0	0	0
4-year	25	92.0% (23/25)	88.0% (22/25)	88.0% (22/25)	88.0% (22/25)	84.0% (21/25)	88.0% (22/25)	88.0% (22/25)	0	0	0	0
5-year	25	84.0% (21/25)	72.0% (18/25)	80.0% (20/25)	84.0% (21/25)	88.0% (22/25)	72.0% (18/25)	72.0% (18/25)	2	0	0	0

Note: In patients experiencing renal failure and unable to undergo contrast-enhanced CT scan, a duplex ultrasound may be used in conjunction with noncontrast CT scan. In these cases, the core laboratory may be able to adequately assess aneurysm size change, endoleak, and patency when an ultrasound is performed in combination with a noncontrast CT scan.
N/A = Not applicable.

3. Summary of Continued Access Results

Procedural Outcomes and Study Outcome Measures

The average estimated procedural blood loss was 237.5 ± 236.4 cc (maximum blood loss was 1000 cc), which was similar to the pivotal cohort (i.e., the average estimated blood loss was 275.6 ± 215.5 cc [maximum blood loss was 800 cc]). The average procedure and total fluoroscopy times (incision to incision closure complete) were 139.6 ± 53.5 minutes and 36.7 ± 28.8 minutes, respectively.

The 6-month freedom from patency-related intervention (defined as freedom from a secondary intervention to treat a >60% stenosis of the internal iliac artery [as identified through computed tomography (CT) scan, angiography, or duplex ultrasound and confirmed by core laboratory] associated with clinical symptoms) was 100% (30/30). One procedure was a technical failure due to the intentional occlusion of the internal iliac artery on the same side as ZBIS. However, there were no clinical symptoms resulting from the occlusion of the internal iliac artery, and no further interventions were required. Thus, it was classified as freedom from patency-related intervention. The 30-day freedom from morbidity was 80% (26/30); four patients experienced morbidity index events within 30 days of the procedure. These events included arrhythmias needing new medication, limb thrombosis on the ZBIS side, infections requiring antibiotics, and hospital readmission within 30 days for a pulmonary embolism needing supplemental oxygen at discharge.

Death, and MAEs through 5 years

Early mortality (≤ 30 days) was 0% (0/30). During the 5-year follow-up, death has been reported in three patients (10%, 3/30) with reported causes of MRSA infection of mitral valve in one patient, acute myeloblastic leukemia in one patient, and emphysema, COPD, and lung cancer. No deaths were adjudicated as related to aneurysm repair.

Access site/incision adverse events were reported in two patients (6.7%, 2/30): one patient had an infection requiring antibiotics, and another patient had a seroma that required treatment. Over 5 years, one patient (3.3%, 1/30) had a MI, and another (3.3%, 1/30) had a stroke. There were no reports of renal failure requiring dialysis, bowel ischemia, buttock claudication, or impotence.

4. Secondary Interventions, Conversion, Rupture, Aneurysm Growth, Endoleak, and Device Integrity Outcomes through 5 years

The occurrence of aneurysm growth, endoleak, device migration, device integrity, and graft patency over a five-year period were evaluated and reported based on core laboratory findings.

Secondary Interventions: Six patients (20%, 6/30) underwent 11 secondary interventions: four on the same side as the ZBIS, three on the side opposite the ZBIS, and four in the aorta. Three patients (10%, 3/30) received secondary interventions: balloon angioplasty, stent placement for a Type III endoleak, and

balloon angioplasty/thrombectomy/stent placement/iliac leg extension on the same side as ZBIS. Two patients underwent stent placement, left iliac limb relining, and coil embolization with ancillary component placement on the side opposite the ZBIS. Two patients underwent balloon angioplasty and fenestrated graft placement followed by coil and glue embolization in the aorta.

Conversion to Open Surgery: There were no conversions to open repair reported through five years.

Aneurysm Growth: Only one common iliac artery aneurysm enlargement (>5 mm) was experienced by one patient (3.3%, 1/30) at the 5-year follow-up.

Endoleak: Throughout the 5-year follow-up schedule, 3 patients (10.0%, 3/30) experienced Type I endoleaks and 1 patient (3.3%, 1/30) experienced a Type III endoleak. Details on the endoleak events are as follows. One patient presented with a distal Type I endoleak involving the iCAST stent at 30 days which persisted at the 6-month follow-up. This event was resolved with a secondary intervention involving stent placement in the internal iliac artery. This same patient had another distal Type I endoleak involving the iliac leg graft on the side opposite the ZBIS at 30 days which persisted at 6-month follow-up. No secondary intervention was performed for this endoleak. Another patient presented with a proximal Type I endoleak involving the AAA main body device (i.e., unrelated to the ZBIS) at the 2-year follow-up. This endoleak (and subsequent AAA growth) was treated with a secondary intervention involving placement of a fenestrated EVAR device. A third patient presented with a Type III endoleak involving the iliac devices on the side opposite the ZBIS at the 2-year follow-up. This endoleak was treated with a secondary intervention involving iliac limb placement. This same patient presented with a distal Type I and a Type III endoleak again involving the iliac devices on the side opposite the ZBIS at the 4-year follow-up. These endoleaks were treated with a secondary intervention involving coil embolization and ancillary component placement.

Device Migration: At the 12-month follow-up, one patient (3.3%, 1/30) experienced migration between the iliac leg graft and distal cuff (non-investigational devices) on side opposite ZBIS, which remained through 5 years. The migration required multiple interventions, the first involving relining of the iliac limb (side opposite ZBIS) and the second involving coil embolization and ancillary component placement (side opposite ZBIS). No migration instances involving the ZBIS were observed.

Device Integrity: No device integrity events involving the study devices were reported throughout the duration of the study.

Aortic Rupture: No ruptures have been reported through 5 years.

Graft Patency: Four occlusions were reported in three patients (10.0%, 3/30) involving various segments of the ZBIS. Specifically, two occlusions occurred within the external iliac artery segment of the ZBIS, and two occlusions were within the internal iliac artery segment of the ZBIS, with both persisting through

the 5-year follow-up. One patient had an external iliac artery occlusion in the ZBIS, requiring thrombectomy and angioplasty. Another experienced a technical failure at procedure requiring internal iliac artery occlusion due to cannulation failure and iCAST stent deployment issues, leading to an Amplatzer plug placement and a persistent occlusion after 5 years. A third patient showed occlusions in the iliac leg graft, ZBIS, and iCAST stent at 2 years, necessitating secondary intervention. The subsequent stent placement intentionally covered the side branch of the ZBIS and iCAST stent, leading to a permanent occlusion of the internal iliac artery at the 5-year mark.

Overall, the clinical outcomes from the continued access study provide additional support for the safety and effectiveness of the ZBIS and iCast for its intended use.

Supplementary Global and Investigational Use

In addition to the pivotal study and continued access cohort data, the Zenith® Iliac Branch has been available OUS since 2006 with over 32,000 implants globally. The device has been studied in an OUS post-market observational registry (27 implants). In the US, the device has been studied in numerous Sponsor-Investigator IDE studies (55 implants). The information available from those sources further supports the safety and effectiveness of the Zenith® Iliac Branch.

XIII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

The primary endpoint for the pivotal study was the assessment of 6-month freedom from patency-related intervention. The success rate was 100% (39/39), which statistically exceeded the performance goal.

The powered safety endpoint for the pivotal study was 30-day freedom from morbidity (i.e., the morbidity index). The success rate for the secondary safety endpoint was 85% (34/40) of subjects, which statistically exceeded the performance goal. The six subjects which did not meet the safety endpoint was due to one event each of distal embolization resulting in tissue loss or requiring reintervention, inotropic support, pneumonia requiring antibiotics, paralytic ileus > 4 days, impotence, and limb thrombosis on the same side as the ZBIS. Additional evidence supporting the safety of the device from the pivotal study includes:

- Low number of SAEs through 30 Days (80% freedom from 30-day

SAE).
- No aneurysm related mortality, ruptures, or conversions through study completion.

Key secondary effectiveness outcomes are described below:
- Technical success was achieved in 100% (40/40) of subjects.
- 6-month internal iliac branch vessel patency was 100% (37/37).
- Procedural success (evaluated at 6-months) was achieved in 87.5% (35/40) of study subjects. Major complications (impotence, ileus, and lower extremity ischemia) were reported for 3 subjects and occlusion of the ZBIS in the external iliac segment was reported in 2 subjects.
- 4 subjects had secondary interventions on the same side of the ZBIS (6 interventions total) through study completion. These interventions most commonly involved placement of an additional stent for the treatment of an occlusion, thrombosis, or endoleak and often treated with minimally invasive or endovascular techniques.
- No device migrations or device integrity issues (e.g., fracture, separation) were reported through study completion.

B. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The anticipated benefit to a patient implanted with the ZBIS device is a minimally invasive approach for treatment of their aortoiliac or iliac aneurysm with a lower risk of operative mortality and other safety outcomes as compared to published outcomes on open surgery. In addition, treatment with ZBIS is anticipated to minimize sequelae associated with loss of blood flow to the internal iliac artery.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The anticipated risks to a patient are the adverse events described above. The probability of 30-day freedom from morbidity following ZBIS implantation is higher than the expected probability of these events following open surgical repair or intentional occlusion of the internal iliac artery during endovascular repair.

Additional factors to be considered in determining risks and benefits for the Zenith® Iliac Branch include:
- Limited clinical study results for female subjects,
- Limited data on patients treated bilaterally with the ZBIS device, and
- Limited data on patients treated with ZBIS as the iliac component of the Zenith Fenestrated proximal aortic component.

Based on the totality of clinical and non-clinical data and probable benefits for patients accessing this device, it was determined that additional testing to support

several chronic biocompatibility endpoints could be appropriately deferred to the post-market.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks for using ZBIS for endovascular treatment of aortoiliac or iliac aneurysms to preserve the internal iliac arterial perfusion in adult patients with morphology suitable for endovascular repair.

1. Patient Perspectives
   This submission did not include specific information on patient perspectives for this device.

C. Overall Conclusions

The non-clinical and clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The 5-year results from the PRESERVE pivotal study, as well as the supplemental 5-year results on the continued access cohort, demonstrate that the ZBIS device is safe and effective for endovascular treatment of aortoiliac or iliac aneurysms to preserve the internal iliac arterial perfusion in adult patients with morphology suitable for endovascular repair.

XII. CDRH DECISION

CDRH issued an approval order on May 30, 2025. The final conditions of approval cited in the approval order are described below.

- Cook has agreed to provide a Clinical Update to physician users at least annually. This clinical update, which can be combined with information on the other marketed Zenith AAA devices, should also include a brief description of any Class I and II recalls, links to any safety communications and descriptions of any field safety notices sent by the sponsor to physician users worldwide. Additional learnings from commercial experience within and outside the United States, a summary of any explant analysis findings and a high-level discussion of any critical publications that discuss safety and performance of the device is also to be included. The clinical update for physician users and the information supporting the updates must be provided in the Annual Report.

- Post-market assessment of chronic biocompatibility endpoints: Chemical characterization and toxicological risk assessment will be performed to address chronic toxicity and carcinogenicity of the Zenith® Iliac Branch. Test protocols will be provided to FDA within 30 days of PMA approval and final reports will be provided to FDA within 12 months of protocol agreement.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIII. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.