6. Summary of Clinical Data

The Zenith® Alpha™ Thoracic Endovascular Graft is indicated for the endovascular treatment of patients with aneurysms or ulcers of the descending thoracic aorta having vascular morphology suitable for endovascular repair.

The Zenith Alpha™ Thoracic Endovascular Graft has been the subject of several documented clinical evaluations, including two pivotal studies (one international) that evaluated the safety and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft in patients with thoracic aneurysm/ulcer and blunt thoracic aortic injury (BTAI), as summarized in Table 6-1. It should be noted that while the study to evaluate use of the device for the treatment of patients with BTAI initially supported approval for an indication inclusive of BTAI in September 2015, subsequent results from longer-term follow-up in combination with results from commercial use suggest an increased risk for in-graft thrombus with use of the device to treat patients with BTAI (refer to the Annual Clinical Update available at www.cookmedical.com for a complete summary of this information). Therefore, the indication for BTAI was removed in June 2017. Additional clinical evaluations include a continued access study for the aneurysm/ulcer indication (see Section 6.2.1) and a European post-market survey (see Section 6.2.2) to further confirm performance of a user interface modification to the introduction system (rotation handle).

Table 6-1. Summary of primary pivotal studies

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

6.1. Clinical Study for the Aneurysm/Ulcer Indication (Through 2 Years)

The Zenith Alpha™ Thoracic Endovascular Graft clinical study was a prospective, nonrandomized, single-arm, multinational study that was conducted to evaluate the safety

and effectiveness of the Zenith Alpha™ Thoracic Endovascular Graft for the treatment of patients with aneurysms/ulcers of the descending thoracic aorta. Patients were treated between March 17, 2010 (first US enrollment on October 1, 2010) and January 16, 2013. The data presented herein was collected on 110 patients through April 7, 2015. There were 23 investigational sites, including centers in the US (51 patients at 14 sites), Japan (43 patients at 3 sites), Germany (13 patients at 4 sites), Sweden (3 patients at 1 site), and England (1 patient at 1 site). The presenting anatomy, based on core laboratory analysis of pre-procedure imaging, was a thoracic aneurysm in 81.8% (90/110) of patients and a thoracic ulcer in 18.2% (20/110) of patients.

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

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

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

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

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

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

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

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

Table 6.1-1. Study follow-up schedule

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

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

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

data presented in this section include the final data through 2 years (730 days). Table 6.1-2 reports the percent of follow-up data available through 2 years for the pivotal cohort.

Table 6.1-2. Follow-up availability

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Clinical Assessment	CT[c]	X-ray	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
Operative	110	100% (110/110)	NA	NA	NA	NA	NA	NA	0	0	0	0
30-day	110	96.4% (106/110)	105/108 (97.2%)	98/108 (90.7%)	105/108 (97.2%)	102/108 (94.4%)	NA	105/108 (97.2%)	3	0	0	2[d]
6-month	105	94.3% (99/105)	96/105 (91.4%)	92/105 (87.6%)	96/105 (91.4%)	91/105 (86.7%)	94/105 (89.5%)	98/105 (93.3%)	2	0	4	0
12-month	99	91.9% (91/99)	92/99 (92.9%)	84/99 (84.8%)	92/99 (92.9%)	83/99 (83.8%)	92/99 (92.9%)	92/99 (92.9%)	7	1	2	0
2-year	89	87.6% (78/89)	79/89 (88.8%)	75/89 (84.3%)	80/89 (89.9%)	76/89 (85.4%)	80/89 (89.9%)	80/89 (89.9%)	4	0	7	0

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

Demographics and Patient Characteristics

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

Table 6.1-3. Demographics and patient characteristics

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

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

Table 6.1-4. Pre-existing comorbid medical conditions

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

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

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

Table 6.1-5 reports the ASA classification.

Table 6.1-5. ASA physical status classification

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

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

Table 6.1-6. SVS-ISCVS risk score classification

SVS-ISCVS Category	Percent Patients (number/total number)
Diabetes risk score	
0	82.7% (91/110)
1	5.5% (6/110)
2	10.0% (11/110)
3	1.8% (2/110)
4	0
Smoking risk score	
0	47.3% (52/110)
1	30.0% (33/110)
2	13.6% (15/110)
3	9.1% (10/110)
Hypertension risk score	
0	11.8% (13/110)
1	29.1% (32/110)
2	31.8% (35/110)
3	27.3% (30/110)
Hyperlipidemia risk score	
0	26.4% (29/110)
1	17.3% (19/110)
2	1.8% (2/110)
3	54.5% (60/110)
Cardiac status risk score	
0	70.0% (77/110)
1	18.2% (20/110)
2	11.8% (13/110)
3	0
Carotid disease risk score	
0	84.5% (93/110)
1	13.6% (15/110)
2	0.9% (1/110)
3	0.9% (1/110)

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

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

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

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

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

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

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

Measure	Mean ± SD (n, range)
Distal neck diameter	
20 mm proximal to celiac artery	
Major (mm)	31.0 ± 5.1 (n=110, 20 – 48)
Minor (mm)	28.9 ± 4.7 (n=110, 19 – 42)
Celiac artery	
Major (mm)	29.5 ± 4.4 (n=110, 20 – 44)
Minor (mm)	27.3 ± 3.8 (n=110, 19 – 38)
Proximal neck length	
Left common carotid artery to distal part of neck (mm)	94.7 ± 57.8 (n=110, 14.4 – 276.7)
Distal neck length	
Celiac artery to proximal part of neck (mm)	105.2 ± 63.2 (n=110, 5.6 – 268.5)
Right iliac artery diameter	
Narrowest segment (mm)	6.7 ± 1.6 (n=105, 3 – 10)[a]
Left iliac artery diameter	
Narrowest segment (mm)	6.9 ± 1.8 (n=104, 0 – 11)[a]

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

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

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

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

[a]Diameter for aneurysms and depth for ulcers.

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

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

Location	Percent Patients (number/total number)
Location in the thoracic aorta	
Proximal	30.0% (33/110)
Middle	50.0% (55/110)
Distal	20.0% (22/110)

Procedural Information

The majority (71.8%) of procedures were performed under general anesthesia, followed by local anesthesia in 21.8% of procedures. Vascular access was gained via femoral artery cutdown in 62.7% of patients, percutaneously in 36.4% of patients and by using a conduit 0.9% of patients. The mean procedure time was 99.4 ± 53.6 minutes (range 31-362 minutes) and the mean procedural blood loss was 121.8 ± 137.7 ml. The mean anesthesia time was 162.6 ± 61.3 minutes and the mean fluoroscopy time was 20.0 ± 20.1 minutes.

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

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

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

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

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

Table 6.1-12. Graft location per core laboratory

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

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

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

Table 6.1-13. Additional procedures

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

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

The device was successfully implanted in 98.2% of patients (2 patients did not receive the device due to the inability to insert/advance the introduction system) and all patients (100%) survived the endovascular procedure. Overall, the procedural results were as expected for the treatment of patients with aneurysms or ulcers of the descending thoracic aorta.

Clinical Utility Measures

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

Table 6.1-14. Clinical utility measures

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

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

Devices Implanted

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

Table 6.1-15. Stent-graft component type deployed

Type	Percent Patients (number/total number)[a]			Graft Diameter Range (All Patients)
	Aneurysm Patients	Ulcer Patients	All patients	
Proximal component (nontapered or tapered)	100% (88/88)	100% (20/20)	100% (108/108)	28 to 46 mm
Distal component	37.5% (33/88)	0	30.6% (33/108)	32 to 46 mm
Ancillary component	27.3% (24/88)[b]	5.0% (1/20)	23.1% (25/108)	28 to 46 mm
Additional proximal component	13.6% (12/88)	5.0% (1/20)	12.0% (13/108)	
Distal extension	14.8% (13/88)[c]	0	12.0% (13/108)	

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

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

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

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

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

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

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

Diameter (mm)	Length (mm)	n
28	132	2
	155	2
30	132	8
	155	2

Diameter (mm)	Length (mm)	n
32	132	7
	155	4
	201	5
34	137	3
	161	6
	209	2
36	137	10
	161	6
	209	1
38	142	7
	167	3
	217	6
40	142	2
	167	3
	217	1
42	121	3
	173	4
44	125	2
	233	1
46	179	4

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

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

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

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

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

Diameter (mm)	Length (mm)	n
32	160	4
	229	1
34	142	2
	190	1

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

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

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

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

Safety Results

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

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

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

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

Death, Rupture, Conversion and MAE

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

Table 6.1-22. Kaplan-Meier estimates freedom from death (all-cause and TAA-related), rupture, conversion, and MAEs (through 730 days)

Event	Parameter	30 Days			180 Days			365 Days			730 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
All-cause mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	2	1	3	4	1	5	11	1	12
	Cumulative censored[c]	1	0	1	2	0	2	6	1	7	10	1	11
	KM estimate[d]	1.000	1.000	1.000	0.977	0.950	0.972	0.954	0.950	0.953	0.869	0.950	0.884
	Standard error	0.000	0.000	0.000	0.016	0.049	0.016	0.023	0.049	0.021	0.037	0.049	0.032
TAA-related mortality	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[e]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
Rupture	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	0	0	0	0	0	0
	Cumulative censored[c]	1	0	1	4	1	5	10	2	12	21	2	23
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000	0.000
Conversion	Number at risk[a]	89	20	109	86	19	105	80	18	98	69	18	87
	Cumulative events[b]	0	0	0	0	0	0	1[f]	0	1	1	0	1
	Cumulative censored[c]	1	0	1	4	1	5	9	2	11	20	2	22
	KM estimate[d]	1.000	1.000	1.000	1.000	1.000	1.000	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.000	0.000	0.000	0.000	0.000	0.000	0.012	0.000	0.010	0.012	0.000	0.010
MAE[g]	Number at risk[a]	85	20	105	81	19	100	74	18	92	60	18	78
	Cumulative events[b]	4	0	4	7	1	8	12	1	13	24	1	25
	Cumulative censored[c]	1	0	1	2	0	2	4	1	5	6	1	7
	KM estimate[d]	0.956	1.000	0.964	0.922	0.950	0.927	0.864	0.950	0.879	0.722	0.950	0.763
	Standard error	0.022	0.000	0.018	0.029	0.049	0.025	0.037	0.049	0.032	0.049	0.049	0.042

[a]Number of patients at risk at the beginning of the interval.

[b]Total events up to and including the specific interval represents all patients who have had the event. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events in each category.

[c]Total censored patients up to and including the specific interval represents all patients who have met a study exit criteria or for whom data are not available at the specific interval.

[d]At end of interval.

[e]Death due to aspiration pneumonia, which the CEC adjudicated as procedure-related due to the pneumonia having likely been related to a stroke that occurred the day of procedure (1040069).

[f]Conversion to open repair due to aortoesophageal fistula, which was adjudicated by the CEC as TAA-related (1040073).

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

All Adverse Events

Table 6.1-23 presents the percent of patients experiencing adverse events according to organ system category.

Table 6.1-23. Percent of patients experiencing adverse events according to organ system category (through 730 days)

Category	Percent of Patients Experiencing Event (n/N)											
	0-30 Days			31-180 Days			181-365 Days			366-730 Days		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Access site/incision[a]	5.6% (5/90)	5.0% (1/20)	5.5% (6/110)	3.4% (3/89)	0	2.8% (3/109)	0	0	0	0	0	0
Cardiovascular[b]	5.6% (5/90)	0	4.5% (5/110)	0	0	0	2.3% (2/86)	0	1.9% (2/105)	1.3% (1/80)	0	1.0% (1/98)
Cerebrovascular/ neurological[c]	3.3% (3/90)	0	2.7% (3/110)	1.1% (1/89)	0	0.9% (1/109)	2.3% (2/86)	0	1.9% (2/105)	0	0	0
Gastrointestinal[d]	1.1% (1/90)	5.0% (1/20)	1.8% (2/110)	4.5% (4/89)	5.0% (1/20)	4.6% (5/109)	1.2% (1/86)	0	1.0% (1/105)	2.5% (2/80)	5.6% (1/18)	3.1% (3/98)
Pulmonary[e]	4.4% (4/90)	0	3.6% (4/110)	1.1% (1/89)	0	0.9% (1/109)	1.2% (1/86)	0	1.0% (1/105)	3.8% (3/80)	0	3.1% (3/98)
Renal[f]	4.4% (4/90)	0	3.6% (4/110)	4.5% (4/89)	0	3.7% (4/109)	3.5% (3/86)	0	2.9% (3/105)	2.5% (2/80)	0	2.0% (2/98)
Vascular[g]	4.4% (4/90)	0	3.6% (4/110)	2.2% (2/89)	5.0% (1/20)	2.8% (3/109)	4.7% (4/86)	0	3.8% (4/105)	10.0% (8/80)	5.6% (1/18)	9.2% (9/98)
Miscellaneous/ other[h]	31.1% (28/90)	35.0% (7/20)	31.8% (35/110)	29.2% (26/89)	20.0% (4/20)	27.5% (30/109)	25.6% (22/86)	15.8% (3/19)	23.8% (25/105)	32.5% (26/80)	27.5% (5/18)	31.6% (31/98)

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

[b]Cardiovascular events included: cardiac arrhythmia (n=4), cardiac arrest (n=0), cardiac ischemia (n=1), congestive heart failure (n=1), myocardial infarction (n=3), and refractory hypertension (n=0).
[c]Cerebrovascular/neurological events included: paralysis (n=0), paraplegia (n=0), paraparesis > 30 days (n=1), spinal cord shock (n=0), transient ischemic attack (n=0), and stroke (n=5).
[d]Gastrointestinal events included: bleeding (n=4), bowel ischemia (n=2), infection (n=4), mesenteric ischemia (n=1), and paralytic ileus > 4 days (n=0).
[e]Pulmonary events included: COPD (n=1), hemothorax (n=0), pleural effusion (n=1), pneumonia (n=6), pneumothorax (n=0), pulmonary edema (n=0), pulmonary embolism (n=1), and pulmonary embolism involving hemodynamic instability or surgery (n=0).
[f]Renal events included: renal failure (n=4), UTI (n=7), serum creatinine rise > 30% above baseline resulting in a persistent value > 2.0 mg/dl (n=2).
[g]Vascular events included: aneurysm (n=11), aortobronchial fistula (n=1), aortoesophageal fistula (n=1), aortoenteric fistula (n=0), coagulopathy (n=1), deep vein thrombosis (n=0), dissection (n=3), embolism (n=2), hematoma (n=1), pseudoaneurysm (n=1), thrombosis (n=1), and vascular injury (n=5).
[h]Miscellaneous/other events included: hypersensitivity/allergic reaction (n=1), multi-organ failure (n=2), sepsis (n=2), and other (n=72).

Effectiveness Results

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

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

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

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

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

Device Performance

Table 6.1-25 presents changes in aneurysm size, as observed from the 30-day (baseline) measurement to each follow-up exam through 2 years (based on core laboratory evaluation). A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Additional details for these patients are provided in the footnotes under Table 6.1-25, which also incorporated the details beyond 2 years to assist in explaining the early-term data (through 2 years) relative to the overall outcome through the course of the study.

Aneurysm growth was associated with endoleak that was noted within 2 years in six patients (1040073, 1030047, 1030051, 1030100, 1040044, and 1040045); all underwent secondary intervention for site-reported reason of endoleak. There was no detectable endoleak in the remaining five patients with aneurysm growth within 2 years, two of whom (1040060 and 1040041) had no change in aneurysm size ($\leq$ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak within 2 years, two required secondary intervention for site-reported reason of progression of disease (1030046, who was first noted to have a distal Type I endoleak by core laboratory subsequent to the secondary intervention) or aneurysm growth (1030017), and one (1030034) had growth.

Aneurysm growth was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing in eight of the 11 patients.

Each of the 11 patients with growth at one or more follow-up time points up to 2 years was initially treated for an aneurysm, often using only a proximal component (n=9), underscoring the importance of adhering to the sizing guidelines in the Instructions for Use (IFU), both in terms of component diameter as well as component type and length, which includes the use of a two-component repair (proximal and distal component) when treating aneurysms.

Table 6.1-25. Change in aneurysm diameter/ulcer depth based on results from core laboratory analysis (through 2 years)

Item	Percent Patients (number/total number)								
	Aneurysm			Ulcer			All		
	6-month	12-month	2-year	6-month	12-month	2-year	6-month	12-month	2-year
Increase (> 5 mm)	4.2% (3/72) [a,b,c]	4.2% (3/71) [a,c,d]	14.3% (9/63)[a,d,e-k]	0	0	0% (0/15)	3.3% (3/90)	3.4% (3/88)	11.5% (9/78)
Decrease (> 5 mm)	19.4% (14/72)	31.0% (22/71)	27.0% (17/63)	33.3% (6/18)	52.9% (9/17)	66.7% (10/15)	22.2% (20/90)	35.2% (31/88)	34.6% (27/78)
No change (≤ 5 mm)	76.4% (55/72)	64.8% (46/71)	58.7% (37/63)	66.7% (12/18)	47.1% (8/17)	33.3% (5/15)	74.4% (67/90)	61.4% (54/88)	53.8% (42/78)

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

[a]Patient 1030046 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted by the core laboratory at the 5-year follow-up (Table 6.3.2.1-6). The patient demonstrated an increase in aneurysm size (compared to baseline) from the 6-month through 5-year follow-ups (Table 6.3.2.1-7). The patient underwent a secondary intervention (proximal component and distal extension placement) 594 days post-procedure for the site-reported reason of progression of disease (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a proximal seal length < 20 mm. The patient has since exited the study.

[b]Patient 1040060 – The patient was treated at the time of the index procedure with two proximal components and one distal component. Per core laboratory evaluation, no endoleaks have been identified in this patient. The patient did not require a secondary intervention. Aneurysm size was stable at 12 months (< 5 mm increase). The patient has since exited the study.

[c]Patient 1040073 – The patient was treated at the time of the index procedure with a single proximal component. The patient had a Type IIb endoleak noted at the 1-month and 6-month follow-ups. The patient demonstrated an increase in aneurysm size at the 6-month and 12-month follow-ups. The patient underwent a secondary intervention (NBCA embolization) 296 days post-procedure for the site-reported reason of Type II endoleak (Table 6.1-30). The patient underwent conversion to open repair 330 days post-procedure (Table 6.1-22) and exited the study 30 days later per the protocol.

[d]Patient 1030017 – The patient was treated at the time of the index procedure with a single proximal component. The patient had no evidence of detectable endoleak. The patient demonstrated an increase in aneurysm size from the 12-month through 5-year follow-ups (Table 6.3.2.1-7). The patient underwent a secondary intervention (distal component placement) 922 days post-procedure for the site-reported reason of aneurysm growth (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient has since exited the study.

[e]Patient 1040034 – The patient was treated at the time of the index procedure with a proximal component and a distal component. The patient did not experience endoleak but demonstrated an increase in aneurysm size at the 2-year, 4-year, and 5-year follow-ups (Table 6.3.2.1-7). No secondary intervention has been performed. The patient has since exited the study.

[f]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 12-month follow-up (and again at an unscheduled CT scan 596 days post procedure) and the 2-year follow-up (Table 6.1-26). The patient demonstrated an increase in aneurysm size and CEC-confirmed migration first noted at an unscheduled visit between the 1-year and 2-year follow-up (Table 6.1-27). The patient underwent a secondary intervention (distal extension placement) 727 post-procedure for the site-reported reasons of persistent distal Type I endoleak and device migration (Table 6.1-30). No growth was noted at 3-years. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient has since exited the study due to death.

[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak (Table 6.1-26) and an increase in aneurysm size were noted at the 2-year follow-up. The patient underwent a secondary intervention (proximal and distal component placement) 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing. The patient has since exited the study.
[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIb endoleak was identified at the 1-month and 6-month follow-ups and a distal Type I endoleak was identified at the 2-year follow-up (Table 6.1-26). The patient demonstrated an increase in aneurysm size at the 2-year, 3-year, and 4-year follow-ups (Table 6.3.2.1-7). The patient underwent a secondary intervention (distal extension placement) 984 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.
[i]Patient 1040041 – The patient was treated at the time of the index procedure with a single proximal component. The patient did not experience endoleak but did demonstrate an increase in aneurysm size at the 2-year follow-up. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient withdrew from the study 906 days post-procedure.
[j]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had a distal Type I endoleak (Table 6.1-26), an increase in aneurysm size, and CEC-confirmed migration (Table 6.1-27) at the 2-year follow-up visit. The patient underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing. The patient has since exited the study.
[k]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month, 2-year, 4-year, and 5-year follow-ups (Table 6.1-26 and Table 6.3.2.1-6.). A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. The patient demonstrated an increase in aneurysm size at the 2-year through 5-year follow-ups (Table 6.3.2.1-7). The patient underwent a secondary intervention (distal component placement) 1827 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

Endoleaks classified by type, as assessed by the core laboratory at each exam period through 2 years, are reported in Table 6.1-26. In total, there were seven patients found to have a Type I (distal) endoleak and two patients found to have a Type III (nonjunctional) endoleak at one or more time points, two of whom (one with Type I and one with Type III) had no evidence of the same endoleak at last available follow-up and without the patients having undergone secondary intervention. Endoleak in the other seven patients (all subsequently required secondary intervention) was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing, which occurred following aneurysm treatment with only a proximal component in six of the patients, underscoring the importance of adhering to the sizing guidelines in the IFU, both in terms of component diameter as well as component type and length, including the use of a two-component repair (proximal and distal components) when treating aneurysms. Additional details for these

patients are provided in the footnotes under Table 6.1-26, which also incorporated the details beyond 2 years to assist in explaining the early-term data (through 2 years) relative to the overall outcome through the course of the study.

Table 6.1-26. Endoleak based on results from core laboratory analysis (through 2 years)

Type	Percent Patients (number/total number)											
	1-month			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Any (new only)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	4.1% (3/73)	5.6% (1/18)	4.4% (4/91)	4.5% (3/66)	0	3.6% (3/83)	8.2% (5/61)	0	6.6% (5/76)
Any (new and persistent)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	11.0% (8/73)	11.1% (2/18)	11.0% (10/91)	10.6% (7/66)	0	8.4% (7/83)	16.4% (10/61)	0	13.2% (10/76)
Multiple	2.4% (2/82)[a]	0	2.0% (2/102)	2.7% (2/73)[a]	0	2.2% (2/91)	1.5% (1/66)	0	1.2% (1/83)	0	0	0
Proximal Type I	0	0	0	0	0	0	0	0	0	0	0	0
Distal Type I (new and persistent)	2.4% (2/82)[a,b]	0	2.0% (2/102)	4.1% (3/73)[a,b,d]	0	3.3% (3/91)	4.5% (3/66)[b,d,e]	0	3.6% (3/83)	8.2% (5/61)[b,e,g-i]	0	6.6% (5/76)
Number new	2	0	2	1	0	1	1	0	1	3	0	3
Type II	7.3% (6/82)[a]	0	5.9% (6/102)	9.6% (7/73)[a,b]	5.6% (1/18)	8.8% (8/91)	6.1% (4/66)[b,j]	0	4.8% (4/83)	6.6% (4/61)[j]	0	5.3% (4/76)
IIa	2	0	2	1	0	1	1	0	1	2	0	2
IIb	4	0	4	5	0	5	2	0	2	2	0	2
Unknown	0	0	0	1	1	2	1	0	1	0	0	0
Type IIIb (new and persistent)	0	5.0% (1/20)[c]	1.0% (1/102)	0	5.6% (1/18)[c]	1.1% (1/91)	1.5% (1/66)[f]	0	1.2% (1/83)	0	0	0
Number new	0	1	1	0	0	0	1	0	1	0	0	0
Type IV	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	1.2% (1/82)	5.0% (1/20)	2.0% (2/102)	0	0	0	0	0	0	1.6% (1/61)	0	1.3% (1/76)

Note: Type IIa = flow from subclavian, celiac, and/or anomalous vertebral arteries; Type IIb = flow from bronchial and/or intercostal arteries.

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

[b]Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month, 2-year, 4-year, and 5-year follow-ups (Table 6.3.2.1-6). A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. The

patient also had aneurysm growth at the 2-year through 5-year follow-ups (Table 6.1-25 and Table 6.3.2.1-7). The patient underwent a secondary intervention (distal component placement) 1827 days post-procedure for the site-reported reason of persistent distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

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

[d]Patient 1030072 – The patient was treated at the time of the index procedure with a proximal component, a distal component, and a distal extension. A distal Type I endoleak was noted at the 6-month and 12-month follow-ups. The patient has not experienced an increase in aneurysm size. The patient underwent a secondary intervention (additional distal extension placement and balloon angioplasty) 420 post-procedure for the site-reported reason of distal Type I endoleak (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.

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

[f]Patient 1030095 – The patient was treated at the time of the index procedure with a single proximal component. A Type III (nonjunctional) endoleak was noted at the 12-month follow-up. The patient has not experienced an increase in aneurysm size. The patient underwent a secondary intervention (distal component placement) 534 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) in combination with the site-reported reason for secondary intervention (distal Type I, not Type III, endoleak) suggest graft undersizing. The patient has subsequently withdrawn from the study 695 days post-procedure.

[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 2-year follow-up. The patient also had aneurysm growth at the 2-year follow-up (Table 6.1-25). The patient underwent a secondary intervention (proximal and distal component placement) 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing. The patient has since exited the study.

[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. A Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak was identified at the 2-year follow-up. The patient demonstrated an increase in aneurysm size at the 2-year, 3-year, and 4-year follow-ups (Table 6.1-25 and Table 6.3.2.1-7). The patient underwent a secondary intervention (distal extension placement) 984 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

[i]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was identified at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1- 25) and CEC-confirmed migration (Table 6.1-27) at the 2-year follow-up visit. The patient underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing. The patient has since exited the study.

[j] Patient 1040036 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIa endoleak was noted at the 12-month, 2-year, and 3-year follow-ups (Table 6.1-26 and Table 6.3.2.1-6). Lengthening of the distal aorta and an increase in aneurysm diameter from 59 mm at the 1-month follow-up to 63 mm at the 3-year follow-up was also noted, likely owing to the distal Type I endoleak (and aneurysm growth) subsequently noted at the 4-year and 5-year follow-ups (Table 6.3.2.1-7). This patient also underwent pre-planned endovascular treatment of an AAA 46 days post-procedure. The patient has since exited the study.

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

Table 6.1-27. Percent of patients (aneurysm and ulcer) with CEC-confirmed migration (date of first occurrence) (through 2 years)

Item	Percent Patients (number/total number)		
	6-month	12-month	2-year
Migration (> 10 mm)	0% (0/98)	0% (0/92)	3.8% (3/80)[a,b,c]

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

[b]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at an unscheduled visit between the 1-year and 2-year follow-ups. The patient also had aneurysm growth (Table 6.1-25), distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention（distal extension placement) 727 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient has since exited the study due to death.

[c]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had aneurysm growth (Table 6.1-25), a distal Type I endoleak (Table 6.1-26), and underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing. The patient has since exited the study.

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

Table 6.1-28. Core laboratory reports of graft kink/compression (through 2 years)

Item	30-day	6-month	12-month	2-year
Kink/compression	0	0	0	1.3% (1/80)[a]

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

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

Table 6.1-29. CEC-confirmed loss of device integrity (through 2 years)

Finding	Percent Patients (number/total number)											
	30-day			6-month			12-month			2-years		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Barb separation	0	0	0	0	0	0	0	0	0	0	0	0
Stent fracture	1.2% (1/85)[a]	0	1.0% (1/105)	1.3% (1/80)[a]	0	1.0% (1/98)	1.3% (1/75)[a]	0	1.1% (1/92)	1.5% (1/65)[a]	0	1.3% (1/80)
Component separation	0	0	0	0	0	0	0	0	0	0	0	0

[a]Patient 1030069 – Patient had a report of a single stent fracture (of the second covered stent in the proximal device) seen on the 30-day, 6-month, 12-month and 2-year x-rays. Nothing uncharacteristic regarding the anatomy or deployment of the graft was observed. This patient has had no clinical sequelae from the stent fracture. The patient withdrew from the study 1153 days post-procedure.

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

Table 6.1-30. Site-reported reasons for secondary intervention (all patients) (through 730 days)

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

[a]Patient 1040058 (ulcer) – Patient had pre-planned left subclavian artery embolization and right-to-left subclavian artery bypass 7 days after the index procedure.
[b]Patient 1040073 (aneurysm) – Patient had two separate secondary interventions for Type II endoleak: unsuccessful attempt at placing embolization coils in the intercostal artery, followed by successful direct puncture of the aneurysm with delivery of N-butyl cyanoacrylate 296 days post-procedure.
[c]Patient 1040037 (aneurysm) – Patient had additional component placed for aortic dissection proximal to the study device 324 days post-procedure.
[d]Patient 1030072 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal extension placement and balloon angioplasty 420 days post-procedure.
[e]Patient 0467042 (aneurysm) – Patient had a dissection distal to the most distal stent treated with distal extension placement 433 days post-procedure.
[f]Patient 1030046 (aneurysm) – Patient had observed progression of disease treated with additional proximal and distal extension placement 594 days post-procedure.
[g]Patient 1030047 (aneurysm) – Patient had distal Type I endoleak and device migration treated with distal extension placement 727 days post-procedure.
[h]Patient 1030095 (aneurysm)– Patient had a persistent Type I distal endoleak treated with additional distal extension placement 534 days post-procedure.
[i]Patient 1040054 (aneurysm) – Patient had a persistent Type IV endoleak per site analysis (unknown type endoleak per core laboratory analysis) treated with extension placemen 599 days post-procedure.

Table 6.1-31. Types of secondary interventions (through 730 days)

Type*	0-30 Days	31-180 Days	181-365 Days	366 – 730 Days
Percutaneous				
Ancillary component placed	0	0	1[b]	6[d-i]
Balloon angioplasty	0	0	0	1[d]
Coil embolization	0	0	0	0
Stent	0	0	0	0
Thrombectomy	0	0	0	0
Thrombolysis	0	0	0	0
Other	0	0	1[b]	0
Surgical				
Conversion to open repair	0	0	0	0
Surgical bypass procedure	0	0	0	0
Other	1[a]	0	0	0
Other	0	0	1[c]	0

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

Gender Subset Analysis

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

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

Summary

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

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

deployment. An access conduit was necessary for graft delivery in 0.9% of patients, and percutaneous access was used in 36.4% of patients.

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

A total of 11 patients experienced aneurysm growth (> 5 mm) at one or more follow-up time points based on core laboratory analysis through 2 years. Aneurysm growth was associated with detectable endoleak in six patients, all of whom underwent secondary intervention. There was no detectable endoleak in the remaining five patients with aneurysm growth, two of whom had no change in aneurysm size (≤ 5 mm change compared to baseline) as of the last available follow-up without the need for secondary intervention. Among the three other patients with growth and no detectable endoleak within 2 years, two required secondary intervention. The majority of patients with aneurysm growth at one or more time points within 2 years (n=9) initially received only a single proximal component, underscoring the importance of adhering to the sizing guidelines in the Instructions for Use (IFU), both in terms of component diameter as well as component type and length, which includes the use of a two-component repair (proximal and distal component) when treating aneurysms.

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

There were three cases of CEC-confirmed migration (two also with aneurysm growth, distal Type I endoleak, and the need for secondary intervention), each of which was associated with an inadequate seal zone length (i.e., length < 20 mm) and/or graft undersizing. There was one report of loss of device integrity (a single stent fracture) within 24 months, but with no adverse clinical sequelae.

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

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

6.2. Summary of Supplemental Clinical Information

6.2.1. Continued Access – Aneurysm/Ulcer Indication (Through 2 Years)

At the completion of enrollment in the pivotal study and prior to commercial availability, the Agency approved continued access to the Zenith® Alpha™ Thoracic Endovascular Graft to investigators under a study expansion that followed the same inclusion/exclusion criteria, follow-up schedule, definitions, and data collection as for the pivotal study. A total of 18 patients were enrolled between April 19, 2013 and January 19, 2015 (12 patients were treated with devices that were packaged in the rotational handle introduction system). The continued access portion of the study was closed to further enrollment following PMA approval by the Agency on September 15, 2015. Table 6.2.1-1 reports the percent of follow-up data available through 2 years for the continued access cohort.

Table 6.2.1-1. Follow-up availability – continued access (through 2 years)

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Clinical Assessment	CT[c]	X-ray	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
Operative	18	100% (18/18)	NA	NA	NA	NA	NA	NA	0	0	0	0
30-day	18	100% (18/18)	94.4% (17/18)	72.2% (13/18)	NA	94.4% (17/18)	NA	100% (18/18)	0	0	0	0
6-month	18	100% (18/18)	100% (18/18)	83.3% (15/18)	100% (18/18)	94.4% (17/18)	94.4% (17/18)	100% (18/18)	0	0	0	0
12-month	18	83.3% (15/18)	72.2% (13/18)	72.2% (13/18)	66.7% (12/18)	66.7% (12/18)	72.2% (13/18)	72.2% (13/18)	3	0	1	0
2-year	14	85.7% (12/14)	71.4% (10/14)	64.3% (9/14)	57.1% (8/14)	71.4% (10/14)	71.4% (10/14)	71.4% (10/14)	0	0	0	0

NA: Not assessed; LTF/WTHD: Lost-to-follow-up/withdrawn; N/A: Not applicable.

[a] Site-submitted data.

[b] Based on core laboratory analysis.

[c] Includes MRI or TEE imaging, which is allowed per protocol when the patient is unable to receive contrast medium.

The following provides an overview of the safety and effectiveness results for the continued access cohort through 2 years.

Mortality: There were three total deaths through 2 years. Two deaths (1030130 and 1030137) were adjudicated as procedure-related by CEC and one (1030141) was unable to be adjudicated (cause of death unknown). Additional details regarding the two TAA-related deaths are as follows: one patient (1030130) died from hemorrhagic shock 351 days post-procedure and the second patient (1030137) died from intra-abdominal bleeding 411 days post-procedure.

Secondary Intervention: One patient (103130) underwent secondary intervention 108 days post-procedure to treat a new site-reported ulcer at the distal end of the proximal component. The patient was treated with an ancillary component and was subsequently noted to have aneurysm growth as well as Type I and Type III endoleaks based on core laboratory analysis of the 6-month follow-up exam without further intervention. The patient presented to the emergency department 350 days post-procedure with hemoptysis and hematemesis and died 351 days post-procedure due to hemorrhagic shock.

Conversion to Open Surgery: There were no conversions to open repair reported through 2 years.

Major Adverse Events (MAEs): There were 5 patients with MAEs through 2 years, including: one wound complication requiring return to operating room and death (1030141), one death (1030130), one stroke (1030142), one re-intubation and death (1030137), and one aneurysm or vessel leak requiring re-operation (1030143).

Aneurysm Growth: Core laboratory-reported increases in aneurysm size (> 5 mm) occurred in three patients through 2 years, each with associated endoleak. One patient (1030130) experienced an increase in aneurysm size at 6 months. This patient also had core laboratory-reported proximal Type I and Type III endoleaks at 6 months, which was subsequent to earlier reintervention involving distal extension placement for the site-reported reason of new ulcer; the patient has since died. One patient (1030141) experienced an increase in aneurysm size at 12 months. The patient also had Type IIa and Type IIb endoleaks. The patient did not undergo a secondary intervention, and has since died. Another patient (1030136) first experienced an increase in aneurysm size at 2 years and continued to experience the increase at 3 years and 4 years. The patient also had core laboratory-reported distal Type I endoleak on subsequent unscheduled follow-up

imaging and underwent a secondary intervention involving additional main body component placement for the site-reported reasons of migration and distal Type I endoleak 959 days post-procedure; this patient has since died.

Endoleak: There were four patients with core laboratory-reported endoleak through 2 years, including one patient with proximal Type I and Type IIIb endoleak (1030130), two patients (1030141 and 1030149) with Type II endoleak (one with IIa and IIb, one IIb), and one patient with Type IIIb and unknown type endoleak (1030124) at one or more scheduled follow-up timepoints within 2 years.

Device Migration: There were no reports of CEC-confirmed migration through 2 years.

Losses of Device Integrity: No CEC-confirmed device integrity observations (barb separation or stent fracture) was identified on the exams analyzed through 2 years.

Aortic Rupture: No ruptures have been reported through 2 years.

Graft Patency: No patients have experienced occlusion through 2 years.

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

A post-market survey was implemented in Europe to gather additional supportive information regarding clinical performance of the rotation handle introduction system. Physician users in Europe were surveyed on the procedural performance of the rotation handle system beginning March 31, 2014. A total of 38 surveys were completed as of June 30, 2014. Table 6.2.2-1 summarizes the survey results.

Table 6.2.2-1. Results of European post-market survey

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

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

All grafts were successfully deployed in the intended location using the primary release sequence, as described in the IFU, with the exception of one report of a slight distal migration during deployment. The alternate release sequence, which is also described in the IFU and is intended to be used in situations in which deployment difficulties involving the handle are encountered, was not used in any case. Furthermore, all grafts were patent at the completion of the procedure and no unique findings were observed as compared to the results from the pivotal clinical studies. These results in combination with the results from the preclinical studies and uses of the introduction system with rotation handle during continued access provide a reasonable assurance of safety and effectiveness of the modifications that were made to the user interface since the time of enrollment completion in the pivotal clinical study.

6.3 Post-Approval Study

6.3.1 Summary of the Post-Approval Study Methods

Data Source

The post-approval study for the Zenith® Alpha™ Thoracic Endovascular Graft involved continued follow-up (through 5 years) of patients enrolled in the premarket pivotal clinical study that was described in Sections 6.1 (for the pivotal study) and 6.2.1 (for the continued access study).

Length of Follow-up and Follow-up Rates

Long-term follow-up (3 - 5 years) availability rates for the pivotal cohort and continued access cohort are reported in Table 6.3.1-1 and Table 6.3.1-2, respectively.

Table 6.3.1-1. Follow-up availability (3-5 years) – pivotal study

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Clinical Assessment	CT[c]	X-ray	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
3-year	78	93.6% (73/78)	91.0% (71/78)	84.6% (66/78)	87.2% (68/78)	80.8% (63/78)	92.3% (72/78)	92.3% (72/78)	1	0	5	0
4-year	72	93.1% (67/72)	93.1% (67/72)	91.7% (66/72)	86.1% (62/72)	83.3% (60/72)	94.4% (68/72)	94.4% (68/72)	6	0	3	0
5-year	63	90.5% (57/63)	85.7% (54/63)	84.1% (53/63)	81.0% (51/63)	69.8% (44/63)	90.5% (57/63)	90.5% (57/63)	N/A[d]	N/A	N/A[e]	N/A

NA: Not assessed; LTF/WTHD: Lost-to-follow-up/withdrawn; N/A: Not applicable.
[a] Site-submitted data.
[b] Based on core laboratory analysis.
[c] Includes MRI or TEE imaging, which is allowed per protocol when the patient is unable to receive contrast medium.
[d] Two patients died > 1825 days after the index procedure.
[e] Four patients were lost to follow-up or withdrew > 1825 days after the index procedure.

Table 6.3.1-2. Follow-up availability (3-5 years) – continued access

Follow-up Visit	Patients Eligible for Follow-up	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval			
		Clinical Assessment	CT[c]	X-ray	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	LTF/ WTHD	Not Due for Next Visit
3-year	14	78.6% (11/14)	78.6% (11/14)	57.1% (8/14)	64.3% (9/14)	71.4% (10/14)	78.6% (11/14)	78.6% (11/14)	2	0	0	0
4-year	12	91.7% (11/12)	83.3% (10/12)	83.3% (10/12)	66.7% (8/12)	66.7% (8/12)	83.3% (10/12)	83.3% (10/12)	3	0	0	0
5-year	9	77.8% (7/9)	77.8% (7/9)	77.8% (7/9)	55.6% (5/9)	77.8% (7/9)	77.8% (7/9)	77.8% (7/9)	N/A[d]	N/A	N/A	N/A

NA: Not assessed; LTF/WTHD: Lost-to-follow-up/withdrawn; N/A: Not applicable.
[a] Site-submitted data.
[b] Based on core laboratory analysis.
[c] Includes MRI or TEE imaging, which is allowed per protocol when the patient is unable to receive contrast medium.
[d] One patient died in the 5-year window and one patient died > 1825 days after the index procedure.

6.3.2 Summary of the Post-Approval Study Results

6.3.2.1 Summary of Final Safety and Effectiveness Findings from the Post-Approval Study (Long-term Results)

This section provides the long-term results for the following endpoints for both the pivotal and continued access cohorts, as identified in the PMA approval order: the rate of adverse events such as death (all-cause), aneurysm-related mortality, secondary interventions, conversion to open surgical repair, major adverse events, endoleak, aneurysm growth, device migration, losses of device integrity, aortic rupture, and graft patency. No formal hypothesis testing was performed for the longer-term follow-up.

All-cause Death

Pivotal

Table 6.3.2.1-1 reports survival from all-cause mortality in the aneurysm and ulcer groups between 3 years (1095 days) and 5 years (1825 days). The survival from all-cause mortality at 1825 days is 75.9% for the overall cohort, 71.3% for the aneurysm group, and 95.0% for the ulcer group. One (1) additional patient died from rupture after 5 years (> 1825 days), which the CEC adjudicated as unrelated.

Table 6.3.2.1-1. Kaplan-Meier all-cause mortality survival estimates – pivotal (3 – 5 years)

Event	Parameter	1095 Days			1460 Days			1825 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
All-cause mortality	Number at risk[a]	60	17	77	52	16	68	46	16	62
	Cumulative events[b]	15	1	16	19	1	20	22	1	23
	Cumulative censored[c]	15	2	17	19	3	22	22	3	25
	KM estimate[d]	0.816	0.950	0.841	0.759	0.950	0.795	0.713	0.950	0.759
	Standard error	0.045	0.049	0.038	0.052	0.049	0.044	0.056	0.049	0.047

[a] Number of patients at risk at the beginning of the interval.
[b] Total events up to and including the specific interval represents all patients who have had the event; includes 12 deaths (11 aneurysm, 1 ulcer) within 730 days.
[c] Total censored patients up to and including the specific interval represents all patients who have met a study exit criterion or for whom data are not available at the specific interval.
[d] At end of interval.

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There were 7 all-cause deaths beyond 2 years (6 patients died between 3-year and 5-year follow-up window, and 1 patient died > 1825 days after the index procedure).

Aneurysm-related Mortality

Pivotal

Table 6.3.2.1-2 summarizes survival from aneurysm-related mortality in the pivotal aneurysm/ulcer study between 3 years (1095 days) and 5 years (1825 days). The survival from aneurysm-related mortality at 1825 days is 99.0% for the overall cohort, 98.8% for the aneurysm group, and 100% for the ulcer group. There has been one TAA-related death reported to date within 5 years, which occurred within 2 years, as previously reported in Section 6.1. In addition, one patient died from rupture after 5 years (> 1825 days); the CEC adjudicated this death as TAA-related, noting an enlarged aneurysm and no intervention. The patient (1030050) was treated at the time of the index procedure with a single proximal component. At 504 days post-procedure, the patient underwent endovascular AAA repair for a newly diagnosed infrarenal aortic aneurysm. At 1852 days post-procedure, the patient presented with back pain and shortness of breath. Findings from CT scan were most consistent with a ruptured thoracic aortic aneurysm. The patient died in transit to the operating room for treatment 1853 days post-procedure. The site-reported cause of death was cardiac arrest.

Table 6.3.2.1-2. Kaplan-Meier aneurysm-related mortality survival estimates (3-5 years)

Event	Parameter	1095 Days			1460 Days			1825 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
TAA-related mortality	Number at risk[a]	60	17	77	52	16	68	46	16	62
	Cumulative events[b]	1	0	1	1	0	1	1	0	1
	Cumulative censored[c]	29	3	32	37	4	41	43	4	47
	KM estimate[d]	0.988	1.000	0.990	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.012	0.000	0.010	0.012	0.000	0.010	0.012	0.000	0.010

[a] Number of patients at risk at the beginning of the interval.
[b] Total events up to and including the specific interval represents all patients who have had the event; includes 1 TAA-related death within 730 days.
[c] Total censored patients up to and including the specific interval represents all patients who have met a study exit criterion or for whom data are not available at the specific interval.
[d] At end of interval.

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There were no CEC-adjudicated aneurysm-related deaths in the continued access portion of the study between 3 years and 5 years, resulting in two CEC-adjudicated aneurysm-related deaths within 5 years in total, both of which occurred within 2 years, as previously reported in Section 6.2.1.

Secondary Interventions

Pivotal

The site-reported reasons for reintervention for pivotal cohort are provided in Table 6.2.3.1-3. Ten new patients underwent secondary intervention between 3 years (1095 days) and 5 years (1825 days). In total, 19 patients have undergone a secondary intervention through 5 years; 11 secondary interventions occurred in patients with core laboratory-observed growth of the treated aneurysm.

Table 6.3.2.1-3. Site-reported reasons for secondary intervention (3-5 years)

Reason	731-1095 Days	1096-1460 Days	1461-1825 Days	> 1825 Days
Device migration	2[a,b]	0	0	0
Endoleak				
Type I proximal	0	0	1[g]	0
Type I distal	4[a-d]	1[f]	0	1[i]
Type II	0	0	0	0
Type IV (through graft body)	0	0	1[h]	0
Other	1[e]	0	0	1[j]

[a] Patient 1030051 (aneurysm) – The patient had persistent distal Type I endoleak and device migration treated with proximal component and distal extension placement 753 days post-procedure.
[b] Patient 1040044 (aneurysm) – The patient had persistent distal Type I endoleak and device migration (confirmed by the CEC) treated with distal extension placement 798 days post-procedure.
[c] Patient 1030100 (aneurysm) – The patient had persistent distal Type I endoleak treated with additional distal extension placement 984 days post-procedure.
[d] Patient 1030089 (aneurysm) – The patient had persistent distal Type I endoleak. (The core laboratory confirmed endoleak on an unscheduled visit after the 2-year visit. The core laboratory was unable to confirm endoleak on the 2-year visit due to a noncontrast CT scan being performed; however, due to enlarging TAA and lack of distal seal, the core laboratory suggested that a distal Type I endoleak was inferred at the 2-year visit.) The patient was treated with additional distal extension placement 990 days post-procedure.
[e] Patient 1030017 (aneurysm) – The patient had aneurysm growth without evidence of endoleak treated with distal extension placement 922 days post-procedure.
[f] Patient 1040024 (aneurysm) – The patient had persistent distal Type I endoleak (identified by the site during a secondary intervention; the core laboratory was unable to determine presence or absence of Type I endoleak due to an incomplete imaging angiogram) treated with additional proximal component and distal extension placement 1212 days post-procedure.
[g] Patient 0467909 (aneurysm) – The patient had proximal Type I endoleak (identified by the site; the core laboratory identified a Type IIa endoleak) treated with proximal and distal extension placement 1576 days post-procedure.
[h] Patient 0460145 (aneurysm) – The patient had aneurysm growth at 4 years (8 mm by site, 9 mm by core laboratory) and 5 years (10 mm by site, 12 mm by core laboratory), which the site attributed to persistent Type IV endoleak (first noted by the site at 4 years). The core laboratory did not identify any endoleaks and could not identify a cause for aneurysm growth. The patient was treated with additional stent-graft placement 1719 days post-procedure.
[i] Patient 1040045 (aneurysm) – The patient had persistent distal Type I endoleak and an increase in aneurysm size treated with distal extension placement 1827 days post-procedure.

[j] Patient 1030052 (aneurysm) – The patient had distal Type I endoleak treated with additional component placement 1862 days post-procedure.

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Three patients underwent secondary intervention between 3 years (1095 days) and 5 years (1825 days) as follows, resulting in four total patients who required a secondary intervention through the course of the study. Secondary intervention in patient 1030136 occurred at 959 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration. The patient was treated with balloon angioplasty and an additional proximal component and distal extension. The patient died 1714 days post-procedure as a result of a fall. Secondary intervention in patient 1030143 occurred 1730 days post-procedure for the site-reported reasons of device separation and Type III endoleak. The core laboratory commented that the endoleak was caused by the loss of overlap between the two devices due to aortic elongation. The patient was treated with a distal extension (above the celiac artery) and balloon angioplasty. The patient completed the study follow-up and exited the study. The secondary intervention in patient 1030144 occurred 1930 days post-procedure for the site-reported reason of persistent proximal and distal Type I endoleak. The patient was treated with an additional proximal component, left carotid to subclavian bypass, and coil embolization. The patient completed the study follow-up and exited the study.

Conversion to Open Surgical Repair

Pivotal

Table 6.3.2.1-4 summarizes the freedom from conversion to open surgical repair in the pivotal study between 3 years (1095 days) and 5 years (1825 days). There were no new reports of conversion to open surgical repair in the pivotal cohort beyond 2 years.

Table 6.3.2.1-4. Kaplan-Meier estimates for freedom from conversion (3-5 years)

Event	Parameter	1095 Days			1460 Days			1825 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Conversion	Number at risk[a]	60	17	77	52	16	68	46	16	62
	Cumulative events[b]	1	0	1	1	0	1	1	0	1
	Cumulative censored[c]	29	3	32	37	4	41	43	4	47
	KM estimate[d]	0.988	1.000	0.990	0.988	1.000	0.990	0.988	1.000	0.990
	Standard error	0.012	0.000	0.010	0.012	0.000	0.010	0.012	0.000	0.010

[a] Number of patients at risk at the beginning of the interval.
[b] Total events up to and including the specific interval represents all patients who have had the event; includes 1 conversion within 730 days.
[c] Total censored patients up to and including the specific interval represents all patients who have met a study exit criterion or for whom data are not available at the specific interval.
[d] At end of interval.

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There were no conversions to open repair reported in the continued access cohort at any timepoint.

Major Adverse Events (MAEs)

Pivotal

Table 6.3.2.1-5 shows the Kaplan-Meier estimates for freedom from MAEs between 3 years (1095 days) and 5 years (1825 days), which were defined as follows: all-cause death; Q-wave myocardial infarction; cardiac event involving arrest, resuscitation, or balloon pump; ventilation > 72 hours or reintubation; pulmonary event requiring tracheostomy or chest tube; renal failure requiring permanent dialysis, hemofiltration, or kidney transplant in a patient with a normal pre-procedure serum creatinine level; bowel resection; stroke; paralysis; amputation involving more than the toes; aneurysm or vessel leak requiring reoperation; deep vein thrombosis requiring surgical or lytic therapy; pulmonary embolism involving hemodynamic instability or surgery; coagulopathy requiring surgery; or wound complication requiring return to the operating room.

Table 6.3.2.1-5. Kaplan-Meier estimates for major adverse events – pivotal (3-5 years)

Event	Parameter	1095 Days			1460 Days			1825 Days		
		Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
MAE	Number at risk[a]	49	16	65	43	15	58	20	9	29
	Cumulative events[b]	31	2	33	35	2	37	43	3	46
	Cumulative censored[c]	10	2	12	12	3	15	27	8	35
	KM estimate[d]	0.634	0.894	0.681	0.581	0.894	0.638	0.470	0.835	0.537
	Standard error	0.054	0.073	0.047	0.057	0.073	0.050	0.058	0.091	0.052

[a] Number of patients at risk at the beginning of the interval.
[b] Total events up to and including the specific interval represents all patients who have had the event; includes 25 patients (24 aneurysm, 1 ulcer) with MAE within 730 days. Note, only the first event is represented in the Kaplan-Meier estimate. A patient may have multiple events.
[c] Total censored patients up to and including the specific interval represents all patients who have met a study exit criterion or for whom data are not available at the specific interval.
[d] At end of interval.

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There were 6 new patients with MAEs between 3 years and 5 years, including 5 deaths (1 patient also with aneurysm or vessel leak requiring re-operation) and 1 patient with aneurysm or vessel leak requiring re-operation. In addition, there were 2 patients with MAE's beyond 5 years (>1825 days), including 1 death and 1 patient with persistent endoleak.

Endoleak

Pivotal

Table 6.3.2.1-6 reports the percentage of patients with endoleak (by type) based on the results from core laboratory analysis. Patients who underwent a secondary intervention for endoleak or who had associated aneurysm size increase are indicated by footnotes, as are any patients with Type I. There were 6 patients who were first noted to have a Type I endoleak between 3 years and 5 years.

In total, there were 13 patients with Type I endoleak through 5 years (all were distal Type I endoleaks, two of which were determined to be unknown endoleak types at subsequent follow-up, while nine were observed in aneurysm patients who did not receive a distal component, whereas it is recommended that aneurysm patients be treated with a proximal and distal component combination), six patients with Type IIa endoleak, eight patients with Type IIb endoleak, two patients with Type II (unknown) endoleak, two patients with Type III endoleak (both Type IIIb), and six patients with unknown endoleak type.

While the focus of the post-approval study was longer-term follow-up (3-5 years), results from earlier timepoints are reproduced below in order to assist in evaluating endoleaks over time.

Table 6.3.2.1-6. Endoleak based on results from core laboratory analysis – pivotal (through 5 years)

Type	Percent Patients (number/total number)																				
	30-day			6-month			12-month			2-year			3-year			4-year			5-year		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Any (new only)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	4.1% (3/73)	5.6% (1/18)	4.4% (4/91)	4.5% (3/66)	0	3.6% (3/83)	8.2% (5/61)	0	6.6% (5/76)	2.0% (1/50)	0	1.6% (1/63)	8.7% (4/46)	0	6.7% (4/60)	11.8% (4/34)	10.0% (1/10)	11.4% (5/44)
Any (new and persistent)	8.5% (7/82)	10.0% (2/20)	8.8% (9/102)	11.0% (8/73)	11.1% (2/18)	11.0% (10/91)	10.6% (7/66)	0	8.4% (7/83)	16.4% (10/61)	0	13.2% (10/76)	10.0% (5/50)	0	7.9% (5/63)	19.6% (9/46)	0	15.0% (9/60)	26.5% (9/34)	10.0% (1/10)	22.7% (10/44)
Multiple	2.4% (2/82)[a]	0	2.0% (2/102)	2.7% (2/73)[a]	0	2.2% (2/91)	1.5% (1/66)	0	1.2% (1/83)	0	0	0	0	0	0	0	0	0	2.9% (1/34)	0	2.3% (1/44)
Proximal Type I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Distal Type I (new and persistent)	2.4% (2/82) [a,b]	0	2.0% (2/102)	4.1% (3/73) [a,b,d]	0	3.3% (3/91)	4.5% (3/66) [b,d,e]	0	3.6% (3/83)	8.2% (5/61) [b,e,g-i]	0	6.6% (5/76)	2.0% (1/50)[j]	0	1.6% (1/63)	4.3% (2/46) [b,k]	0	3.3% (2/60)	17.6% (6/34) [b,k,l,m,n,o]	0	13.6% (6/44)
Number new	2	0	2	1	0	1	1	0	1	3	0	3	1	0	1	1	0	1	4	0	4
Type II	7.3% (6/82)[a]	0	5.9% (6/102)	9.6% (7/73) [a,b]	5.6% (1/18)	8.8% (8/91)	6.1% (4/66) [b,k]	0	4.8% (4/83)	6.6% (4/61)[k]	0	5.3% (4/76)	8.0% (4/50)[k]	0	6.3% (4/63)	8.7% (4/46)	0	6.7% (4/60)	8.8% (3/34)	0	6.8% (3/44)
IIa	2	0	2	1	0	1	1	0	1	2	0	2	3	0	3	1	0	1	1	0	1
IIb	4	0	4	5	0	5	2	0	2	2	0	2	1	0	1	3	0	3	2	0	2
Unknown	0	0	0	1	1	2	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Type IIIb (new and persistent)	0	5.0% (1/20)[c]	1.0% (1/102)	0	5.6% (1/18)[c]	1.1% (1/91)	1.5% (1/66)[f]	0	1.2% (1/83)	0	0	0	0	0	0	0	0	0	0	0	0
Number new	0	1	1	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0
Type IV	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Unknown	1.2% (1/82)	5.0% (1/20)	2.0% (2/102)	0	0	0	0	0	0	1.6% (1/61)	0	1.3% (1/76)	0	0	0	6.5% (3/46)[j]	0	5.0% (3/60)	2.9% (1/34)	10.0% (1/10)	4.5% (2/44)

Note: Type IIa = flow from subclavian, celiac, and/or anomalous vertebral arteries; Type IIb = flow from bronchial and/or intercostal arteries.

[a] Patient 0463776 – The patient was treated at the time of the index procedure with a proximal component and a distal component. Distal Type I and Type IIb endoleaks were noted at the 1-month and 6-month follow-ups. The endoleak type was noted as unknown at the last follow-up (unscheduled follow-up 300 days post-procedure); a decrease in aneurysm size was also noted at the last follow-up. No secondary interventions were performed, and the patient has since withdrawn from the study.

[b] Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12 month, 2-year, 4-year, and 5-year follow-ups. A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups. The patient also had aneurysm growth at the 2-year through 5-year follow-ups (Table 6.1-25 and Table 6.3.2.1-7). The patient underwent a secondary intervention (distal component placement) 1827 days post-procedure for the site-reported reason of persistent distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

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

[d] Patient 1030072 – The patient was treated at the time of the index procedure with a proximal component, a distal component, and a distal extension. A distal Type I endoleak was noted at the 6-month and 12-month follow-ups. The patient has not experienced an increase in aneurysm size. The patient underwent a secondary intervention (additional distal extension placement and balloon angioplasty) 420 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm.

[e] Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 12-month follow-up (and again at an unscheduled CT scan 596 days post-procedure) and the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25) and CEC-confirmed migration (Table 6.1-27) first noted at an unscheduled visit between the 1-year and 2-year follow-ups. The patient underwent a secondary intervention (distal extension placement) 727 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.1-30). There was no endoleak detected at the 3-year follow-up. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient has since exited the study due to death.

[f] Patient 1030095 – The patient was treated at the time of the index procedure with a single proximal component. A Type III (nonjunctional) endoleak was noted at the 12-month follow-up. The patient has not experienced an increase in aneurysm size. The patient underwent a secondary intervention (distal component placement) 534 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) in combination with the site-reported reason for secondary intervention (distal Type I, not Type III, endoleak) suggest graft undersizing. The patient has subsequently withdrawn from the study 695 days post-procedure.

[g] Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 2-year follow-up. The patient also had aneurysm growth at the 2-year follow-up (Table 6.1-25). The patient underwent a secondary intervention (proximal and distal component placement) 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing. The patient has since exited the study.

[h] Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIb endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak was identified at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25). The patient underwent a secondary intervention (distal extension placement) 984 days post-procedure for the site-reported reason of distal

Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

[i] Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was identified at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

[j] Patient 1030107 – The patient was treated at the time of the index procedure with a proximal component and a distal component. A distal Type I endoleak was noted on the procedural angiogram, but was not seen on the 1-month, 6-month, 12-month, or 2-year follow-up CT scans. A distal Type I endoleak was noted on the 3-year CT scan, and an unknown type endoleak was noted on the 4-year CT scan. Review of core laboratory measurements of graft location at first follow-up (relative to the location of actual graft placement) suggests potential graft undersizing.

[k] Patient 1040036 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIa endoleak was noted at the 12-month, 2-year, and 3-year follow-ups. Lengthening of the distal aorta and an increase in aneurysm diameter from 59 mm at the 1-month follow-up to 63 mm at the 3-year follow-up was also noted, likely owing to the distal Type I endoleak (and aneurysm growth) subsequently noted at the 4-year and 5-year follow-ups (Table 6.3.2.1-7). This patient also underwent pre-planned endovascular treatment of an AAA 46 days post-procedure. The patient has since exited the study.

[l] Patient 1030022 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted by the core laboratory at the 5-year follow-up. No secondary interventions were performed, and the patient did not demonstrate an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm and potential graft undersizing. The patient has since exited the study.

[m] Patient 1030046 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted by the core laboratory at the 5-year follow-up. The patient demonstrated an increase in aneurysm size (compared to baseline) from the 6-month through 5-year follow-ups (Table 6.3.2.1-7). The patient underwent a secondary intervention (proximal and distal component placement) 594 days post-procedure for the site-reported reason of progression of disease (Table 6.1-30). Following this secondary intervention, the core laboratory noted that the distal seal zone remained tenuous at the 2-year time point. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a proximal seal length < 20 mm. The patient has since exited the study.

[n] Patient 1030052 – The patient was treated at the time of the index procedure with a proximal component, distal component, and distal extension. A distal Type I endoleak was first noted by the core laboratory at the 5-year follow-up; the core laboratory reported the diameter at the most distal aspect of the graft was notable for an approximate 20 mm increase from 1 month to 5 years. The patient did not demonstrate an increase in aneurysm size during the study. The patient underwent a secondary intervention (distal component placement) 1862 days post-procedure for the site-reported reason of aneurysm growth in the descending thoracic aorta distal to the originally treated segment (Table 6.3.2.1-3). The patient died of aneurysm rupture two days after the intervention, which the CEC adjudicated as not related to the device or procedure.

[o] Patient 1040062 – The patient was treated at the time of the index procedure with two proximal components. A Type IIb endoleak was first noted by the core laboratory at the 1-month follow-up and at each subsequent follow-up through the 5-year follow-up, at which time the core laboratory also noted a distal Type I endoleak. The patient had demonstrated an increase in aneurysm size (compared to baseline) from the 3-year through the 5-year follow-ups (Table 6.3.2.1-7). No secondary interventions were performed. Review of core laboratory measurements of graft location at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

Continued Access

There were four new patients with endoleak first noted between 3 years and 5 years (1030143, 1030136, 1030144, and 1030158), resulting in eight patients with core laboratory-reported endoleak through the course of the study.

In total, there have been five patients (1030124, 1030130, 1030136, 1030144, 1030158) with Type I endoleak (two proximal, one proximal and distal, two distal), three patients (1030124, 1030141, 1030149) with Type II endoleak (one IIa and IIb, one IIb, one subtype unknown), three patients (1030124, 1030130, 1030143) with Type III endoleak (one IIIa, two IIIb), and two patients (1030124, 1030130) with unknown type endoleak at one or more scheduled or unscheduled follow-up timepoints through 5 years.

Aneurysm Growth

Pivotal

Table 6.3.2.1-7 reports the percentage of patients with an increase (> 5 mm), decrease (> 5 mm), or no change (≤ 5 mm) in aneurysm diameter (or ulcer depth) by core laboratory analysis at each follow-up time point subsequent to 1 month, which represents baseline. While the focus of the post-approval study was longer-term follow-up (3-5 years), the results from earlier timepoints (6-month, 1- and 2-years) are reproduced below in order to demonstrate that some patients with an increase in aneurysm diameter during longer-term follow-ups were the same patients who also had an increase in aneurysm diameter at earlier timepoints. There were 9 new patients who had aneurysm growth at one or more follow-up time points between 3 years and 5 years. The first occurrence of growth was observed at 3 years in two patients, at 4 years in four patients, and at 5 years in three patients. Additional details for these patients are provided in the footnotes under Table 6.3.2.1-7. In total, there were 20 patients who experienced aneurysm growth through 5 years.

Secondary interventions for reasons such as growth, endoleak, and/or migration have been reported by the site in 10 patients (0460145, 1030017, 1030046, 1030047, 1030051, 1030100, 1040024, 1040044, 1040045, 1040073) with core laboratory-reported aneurysm growth (one of whom had continued aneurysm growth following reintervention without evidence of endoleak); an additional patient with aneurysm growth (0467042) underwent

reintervention for the site-reported reason of distal dissection. The remaining 9 patients with growth had no secondary interventions prior to exiting the study.

All patients with growth at one or more follow-up time points (n=20) were treated for an aneurysm, often without use of a distal main body component (n=17). Additionally, while the percentage of aneurysm patients enrolled in this study (81.8%) was comparable to that from the previous study for the Zenith® TX2® TAA Endovascular Graft (85.6%), a proximal and distal main body component pair was used in only 37.5% of the aneurysm patients in the present study compared to nearly 70.0% of the aneurysm patients in the previous study, in which 7.0% of patients had aneurysm growth at 5 years. Therefore, the labeling for the Zenith® Alpha™ Thoracic Endovascular Graft was specifically updated subsequent to completion of enrollment in the present study to emphasize the use of a proximal main body component and distal main body component together when treating an aneurysm in order to best ensure adequate fixation and seal proximal and distal to the aneurysm.

Table 6.3.2.1-7. Change in aneurysm diameter/ulcer depth based on results from core laboratory analysis – pivotal (through 5 years)

Item	Percent Patients (number/total number)					
	Aneurysm					
	6-month	12-month	2-year	3-year	4-year	5-year
Increase (> 5 mm)	4.2% (3/72)[a,b,c]	4.2% (3/71)[a,c,d]	14.3% (9/63)[a,d,e-k]	11.5% (6/52)[a,d,h,k-m]	23.4% (11/47)[a,d,e,h,k-q]	33.3% (13/39)[a,d,e,k-t]
Decrease (> 5 mm)	19.4% (14/72)	31.0% (22/71)	27.0% (17/63)	26.9% (14/52)	25.5% (12/47)	17.9% (7/39)
No change (≤ 5 mm)	76.4% (55/72)	64.8% (46/71)	58.7% (37/63)	61.5% (32/52)	51.1% (24/47)	48.7% (19/39)
Item	**Percent Patients (number/total number)**					
	Ulcer					
	6-month	**12-month**	**2-year**	**3-year**	**4-year**	**5-year**
Increase (> 5 mm)	0% (0/18)	0% (0/17)	0% (0/15)	0% (0/13)	0% (0/13)	0% (0/11)
Decrease (> 5 mm)	33.3% (6/18)	52.9% (9/17)	66.7% (10/15)	46.2% (6/13)	53.8% (7/13)	45.5% (5/11)
No change (≤ 5 mm)	66.7% (12/18)	47.1% (8/17)	33.3% (5/15)	53.8% (7/13)	46.2% (6/13)	54.5% (6/11)
Item	**Percent Patients (number/total number)**					
	All					
	6-month	**12-month**	**2-year**	**3-year**	**4-year**	**5-year**
Increase (> 5 mm)	3.3% (3/90)	3.4% (3/88)	11.5% (9/78)	9.2% (6/65)	18.3% (11/60)	26.0% (13/50)
Decrease (> 5 mm)	22.2% (20/90)	35.2% (31/88)	34.6% (27/78)	30.8% (20/65)	31.7% (19/60)	24.0% (12/50)
No change (≤ 5 mm)	74.4% (67/90)	61.4% (54/88)	53.8% (42/78)	60.0% (39/65)	50.0% (30/60)	50.0% (25/50)

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

[a] Patient 1030046 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted by the core laboratory at the 5-year follow-up (Table 6.3.2.1-6). The patient demonstrated an increase in aneurysm size (compared to baseline) from the 6-month through 5-year follow-ups. The patient underwent a secondary intervention (proximal component and distal extension placement) 594 days post-procedure for the site-reported reason of progression of disease (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a proximal seal length < 20 mm. The patient has since exited the study.

[b] Patient 1040060 – The patient was treated at the time of the index procedure with two proximal components and one distal component. Per core laboratory evaluation, no endoleaks have been identified in this patient. Aneurysm size was stable at 12 months (< 5 mm increase). The patient did not require a secondary intervention. The patient has since exited the study.

[c] Patient 1040073 – The patient was treated at the time of the index procedure with a single proximal component. The patient had a Type IIb endoleak noted at the 1-month and 6-month follow-ups. The patient demonstrated an increase in aneurysm size at the 6-month and 12-month follow-ups (Table 6.1-25). The patient underwent a secondary intervention (NBCA embolization) 296 days post-procedure for the site-reported reason of Type II endoleak (Table 6.1-30). The patient underwent conversion to open repair 330 days post-procedure (Table 6.1-22) and exited the study 30 days later per the protocol.

[d] Patient 1030017 – The patient was treated at the time of the index procedure with a single proximal component. The patient had no evidence of detectable endoleak. The patient demonstrated an increase in aneurysm size from the 12-month through 5-year follow-ups. The patient underwent a secondary intervention (distal extension placement) 922 days post-procedure for the site-reported reason of aneurysm growth (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient has since exited the study.
[e] Patient 1040034 – The patient was treated at the time of the index procedure with a proximal component and a distal component. The patient did not experience endoleak but demonstrated an increase in aneurysm size at the 2-year, 4-year, and 5-year follow-ups. No secondary intervention has been performed and the patient has since exited the study.
[f] Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 12-month follow-up (and again at an unscheduled CT scan 596 days post procedure) and the 2-year follow-up (Table 6.1-26). The patient demonstrated an increase in aneurysm size and CEC-confirmed migration first noted at an unscheduled visit between the 1-year and 2-year follow-ups (Table 6.1-27). The patient underwent a secondary intervention (distal extension placement) 727 days post-procedure for the site-reported reasons of persistent distal Type I endoleak and device migration (Table 6.1-30). No growth was noted at the 3-year follow-up. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient has since exited the study due to death.
[g] Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak (Table 6.1-26) and an increase in aneurysm size were noted at the 2-year follow-up. The patient underwent a secondary intervention (proximal and distal component placement) 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing. The patient has since exited the study.
[h] Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIb endoleak was identified at the 1-month and 6-month follow-ups and a distal Type I endoleak was identified at the 2-year follow-up (Table 6.1-26). The patient demonstrated an increase in aneurysm size at the 2-year, 3-year, and 4-year follow-ups. The patient underwent a secondary intervention (distal extension placement) 984 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.
[i] Patient 1040041 – The patient was treated at the time of the index procedure with a single proximal component. The patient did not experience endoleak but did demonstrate an increase in aneurysm size at the 2-year follow-up (Table 6.1-25). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing as well as a distal seal length < 20 mm. The patient withdrew from the study 906 days post-procedure.
[j] Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had a distal Type I endoleak (Table 6.1-26), an increase in aneurysm size, and CEC-confirmed migration (Table 6.1-27) at the 2-year follow-up visit. The patient underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.
[k] Patient 1040045 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 1-month, 6-month, 12-month, 2-year, 4-year, and 5-year follow-ups (Table 6.3.2.1-6). A Type IIb endoleak was also identified at the 6-month and 12-month follow-ups (Table 6.1-26). The patient demonstrated an increase in aneurysm size at the 2-year through 5-year follow-ups. The patient

underwent a secondary intervention (distal component placement) 1827 days post-procedure for the site-reported reason of distal Type I endoleak and an increase in aneurysm size (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

[l] Patient 1040024 – The patient was treated at the time of the index procedure with a single proximal component. No endoleaks or migration were noted at any follow-up time point. The patient demonstrated an increase in aneurysm size at the 3-year, 4-year, and 5-year follow-ups. At the 6-month follow-up, the core laboratory noted that the distal seal zone was extremely short and the patient was at risk for loss of distal seal. At the 3-year follow-up, the core laboratory noted that the device was in jeopardy of losing the distal seal completely. The patient underwent a secondary intervention (additional proximal component and distal extension (Gore TAG devices) placement) 1212 days post-procedure for the site-reported reason of distal Type I endoleak (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm. The patient has since exited the study.

[m] Patient 1040062 – The patient was treated at the time of the index procedure with two proximal components. A Type IIb endoleak was noted at the 1-month through 5-year follow-ups, with a distal Type I endoleak also noted at the 5-year follow-up (Table 6.3.2.1-6). At the 3-year follow-up, growth of > 5 mm was noted (maximum aneurysm diameter increased by 7 mm from 68 mm at 1 month to 75 mm at 3 years). Aneurysm growth continued to be noted by the core laboratory at the 4-year and 5-year follow-ups. No secondary interventions were performed. The patient has since exited the study.

[n] Patient 0460145 – The patient was treated at the time of the index procedure with a single proximal component. No endoleaks or migration were noted at any follow-up time point. The patient demonstrated an increase in aneurysm size at the 4-year follow-up (8 mm by site, 9 mm by core laboratory). The core laboratory could not identify a cause for aneurysm growth. The patient underwent a secondary intervention (additional stent-graft placement) 1719 days post-procedure for the site-reported reason of Type IV endoleak (first noted at 4 years) (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

[o] Patient 1040017 – The patient was treated at the time of the index procedure with one proximal component and two distal extensions. No endoleak or migration has been noted at any time point. The patient demonstrated an increase in aneurysm size at the 4-year and 5-year follow-ups. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

[p] Patient 1040036 – The patient was treated at the time of the index procedure with a single proximal component. A Type IIa endoleak was noted at the 12-month, 2-year, and 3-year follow-ups (Table 6.3.2.1-6). Lengthening of the distal aorta and an increase in aneurysm diameter from 59 mm at the 1-month follow-up to 63 mm at the 3-year follow-up was also noted, likely owing to the aneurysm growth (and distal Type I endoleak) subsequently noted at the 4-year and 5-year follow-ups. This patient also underwent pre-planned endovascular treatment of an AAA 46 days post-procedure. The patient has since exited the study.

[q] Patient 1040079 – The patient was treated at the time of the index procedure with two proximal components. A Type II endoleak was noted at the 6-month and 12-month follow-ups, a Type IIb endoleak was noted at the 2-year, 4-year, and 5-year follow-ups, and a Type IIa endoleak was noted at the 3-year follow-up. The patient demonstrated an increase in aneurysm size at the 4-year and 5-year follow-ups. No secondary interventions were performed. The patient has since exited the study.

[r] Patient 0467042 – The patient was treated at the time of the index procedure with a proximal component, distal component, and distal extension. A Type IIb endoleak was noted at the 4-year follow-up and a Type IIa endoleak was observed at the 5-year follow-up. Aneurysm growth was noted by the core laboratory at the 5-year follow-up. The patient underwent a secondary intervention (distal extension placement) 433 days post-procedure for the site-reported reason of distal dissection (Table 6.1-30). No secondary intervention for growth was reported. The patient has since exited the study.

[s] Patient 1030102 – The patient was treated at the time of the index procedure with a proximal component and a distal extension. No endoleaks have been noted at any time point. The patient demonstrated an increase in aneurysm size at the 5-year follow-up. The patient did not have a secondary intervention. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm and potential undersizing. Additionally, there was less than the minimum recommended amount of overlap between components initially. The patient has since exited the study.

[t] Patient 1040046 – The patient was treated at the time of the index procedure with two proximal components. No endoleaks have been noted at any time point. The patient demonstrated an increase in aneurysm size at the 5-year follow-up. No secondary interventions have been performed. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests proximal and distal graft undersizing. The patient has since exited the study.

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Core laboratory-reported increases in aneurysm size (> 5 mm) have occurred in two new patients beyond 2 years as follows, thus providing five patients total with aneurysm growth at any time point during continued access.

One patient (1030143) experienced an increase in aneurysm size at 3 years, 4 years, and 5 years. The patient also had core laboratory-reported Type III endoleak at 4 years and underwent a secondary intervention involving ancillary component placement and balloon angioplasty for the site-reported reasons of device separation and persistent endoleak; the patient completed the study follow-up and exited the study. Another patient (1030124) experienced an increase in aneurysm size at 3 years, 4 years, and 5 years. The patient also had core laboratory-reported Type III endoleak at 1 month; unknown type endoleak at 6 months, 12 months, and 5 years; and proximal Type I endoleak at 3 years, 4 years, and 5 years. The patient did not undergo a secondary intervention; the patient completed the study follow-up and exited the study.

Device Migration

Pivotal

There were no new reports of CEC-confirmed migration between 3 years and 5 years, as shown in Table 6.3.2.1-8, which also reproduces results from the earlier timepoints for reference.

Table 6.3.2.1-8. Percent of patients (aneurysm and ulcer) with CEC-confirmed migration (date of first occurrence) – pivotal (through 5 years)

Item	Percent Patients (number/total number)					
	6-month	12-month	2-year	3-year	4-year	5-year
Migration (> 10 mm)	0% (0/98)	0% (0/92)	3.8% (3/80)[a,b,c]	0% (0/72)	0% (0/68)	0% (0/57)

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

[b] Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at an unscheduled visit between the 1-year and 2-year follow-ups. The patient also had distal Type I endoleak (Table 6.1-26), aneurysm growth (Table 6.1-25), and underwent a secondary intervention (distal extension placement) 727 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient has since exited the study due to death.

[c] Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient had cranial migration of the distal end of the proximal component first confirmed by the CEC at 2 years. The patient also had a distal Type I endoleak (Table 6.1-26), aneurysm growth (Table 6.1-25), and underwent a secondary intervention (distal extension placement) 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration (Table 6.3.2.1-3). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing. The patient has since exited the study.

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There was one report of CEC-confirmed migration during continued access, which occurred between 3 years and 5 years. Patient 1030158 was treated with a single proximal component for a thoracic aortic ulcer, which had resolved by the 12-month visit per both the site and core laboratory. From the 3-year follow-up CT scan, the core laboratory noted growth in the aortic diameter just below the original ulcer site. From the 4-year follow-up CT scan, the core laboratory noted continued progression of the aortic diameter to a maximum diameter of 45.8 mm. From the 5-year CT scan, the core

laboratory noted a distal Type I endoleak. Proximal (cranial) migration of the distal end of a proximal component at the 5-year time point was confirmed by the CEC.

Losses of Device Integrity

Pivotal

Table 6.3.2.1-9 reports the CEC-confirmed device integrity observations at each exam period between 3 years and 5 years, noting the only new observation during this period was a single stent fracture in one patient.

Table 6.3.2.1-9. CEC-confirmed loss of device integrity – pivotal (3-5 years)

Finding	Percent Patients (number/total number)								
	3-year			4-year			5-year		
	Aneur	Ulcer	All	Aneur	Ulcer	All	Aneur	Ulcer	All
Barb separation	0	0	0	0	0	0	0	0	0
Stent fracture	1.8% (1/57)[a]	0	1.4% (1/72)	1.9% (1/52)[a]	0	1.5% (1/68)	0	0	0
Component separation	0	0	0	0	0	0	0	0	0

[a] Patient 1030028 – Per the core laboratory, a single fracture of the proximal bare stent of the device was noted on the 3-year and 4-year x-rays. Nothing uncharacteristic regarding the anatomy or deployment of the graft was observed. This patient has had no clinical sequelae from the stent fracture. No secondary interventions were performed, and the patient has since exited the study.

Continued Access

There were no reports of CEC-confirmed device integrity observations (barb separation or stent fracture) between 3 years and 5 years.

Aortic Rupture

Pivotal

No ruptures have been reported in the pivotal cohort within 5 years (1825 days). Two ruptures were reported after 5 years (1030050, 1030052). Details regarding patient 1030050 were described in the Aneurysm-related Mortality section. Details regarding patient 1030052 are as follows: this patient with prior open repair involving the ascending and descending thoracic aorta (secondary to giant cell aortitis) was treated at the time of the index procedure with a proximal component, distal component, and distal extension. On post-operative day 1862, the patient underwent additional thoracic graft

placement due to reported growth in the descending thoracic aorta distal to the originally treated segment. Two days later, the patient died from left hemothorax due to rupture. The CEC adjudicated the death as unrelated, noting there was aneurysm growth below the endograft.

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No ruptures have been reported in the continued access cohort.

Graft Patency

Pivotal

No patients have experienced occlusion. Throughout follow-up, there have been four patients with confirmed presence of thrombus in the graft (three in the setting of excessive graft oversizing, one in the setting of preexisting aortic neck thrombus).

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No patients have experienced occlusion. Throughout follow-up, there have been two patients with confirmed presence of thrombus in the graft (in the setting of preexisting aortic neck thrombus).

6.3.2.2 Study Strengths and Weaknesses

The pivotal clinical study was well controlled, having been conducted in accordance with ISO 14155, 21 CFR 812, JGCP, ICH GCP, and other applicable requirements as appropriate. Additionally, the study utilized an independent core laboratory to ensure uniform analysis of pre-procedure and follow-up imaging exams.

The continued access study followed the same inclusion/exclusion criteria, follow-up schedule, definitions, and data collection as that for the pivotal study, but was not powered to test any study hypotheses.

The comorbid medical conditions of the patient population, which often resulted in death for reasons unrelated to the study aneurysm/device, limited the number of enrolled patients with completed 5-year follow-up.