Summary of Clinical Data

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

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

Table 6-1. Summary of primary pivotal studies

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

6.1. Clinical Study for the Aneurysm/Ulcer Indication

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

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

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

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

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

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

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

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

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

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

Table 6.1-1. Study follow-up schedule

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

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

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

Table 6.1-2. Follow-up availability

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

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

Demographics and Patient Characteristics

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

Table 6.1-3. Demographics and patient characteristics

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

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

Table 6.1-4. Pre-existing comorbid medical conditions

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

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

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

Table 6.1-5 reports the ASA classification.

Table 6.1-5. ASA physical status classification

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

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

Table 6.1-6. SVS-ISCVS risk score classification

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

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

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

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

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

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

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

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

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

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

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

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

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

[a]Diameter for aneurysms and depth for ulcers.

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

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

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

Procedural Information

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

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

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

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

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

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

Table 6.1-12. Graft location per core laboratory

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

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

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

Table 6.1-13. Additional procedures

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

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

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

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

Clinical Utility Measures

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

Table 6.1-14. Clinical utility measures

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

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

Devices Implanted

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

Table 6.1-15. Stent-graft component type deployed

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Safety Results

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

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

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

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

Death, Rupture, Conversion and MAE

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

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

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

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

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

All Adverse Events

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

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

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

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

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

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

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

Effectiveness Results

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

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

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

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

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

Device Performance

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

[d]Patient 1030072 – A distal Type I endoleak was noted at the 6-month and 12-month follow-ups. A secondary intervention has occurred (for the site-reported reason of distal Type I endoleak after 12-month follow-up). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. The patient underwent a secondary intervention on post-operative day 420 (Table 6.1-30) and there was no endoleak detected at the 2-year follow-up.
[e]Patient 1030047 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was first noted at the 12-month follow-up (and again at an unscheduled CT (596 days post procedure)) and the 2-year follow-up, at which time the patient underwent secondary intervention. The patient also had aneurysm growth (Table 6.1-25) and CEC-confirmed migration (Table 6.1-27). The patient underwent a secondary intervention (ancillary component placement) 727 days post-procedure (Table 6.1-30). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing and a distal seal length < 20 mm. There was no endoleak detected at the 3-year follow-up.
[f]Patient 1030095 – The patient was treated at the time of the index procedure with a single proximal component. A Type III (nonjunctional) endoleak was noted at the 12-month follow-up (a secondary intervention involving distal component placement was performed after the 12-month follow-up for the site-reported reason of distal Type I endoleak; Table 6.1-30). The patient has not experienced an increase in aneurysm size. Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) in combination with the site-reported reason for secondary intervention (distal Type I, not Type III, endoleak) suggest graft undersizing. Patient has subsequently withdrawn from the study on post-operative day 695.
[g]Patient 1030051 – The patient was treated at the time of the index procedure with a single proximal component. A distal Type I endoleak was noted at the 2-year follow-up. The patient also had aneurysm growth (Table 6.1-25) and underwent a secondary intervention beyond 2 years (ancillary component placement 753 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests a distal seal length < 20 mm as well as graft undersizing.
[h]Patient 1030100 – The patient was treated at the time of the index procedure with a single proximal component. Per core laboratory evaluation, a Type II endoleak was identified at the 1-month and 6-month follow-ups. A distal Type I endoleak has been identified in the patient at 2 years (previous endoleaks identified were Type II). The patient also had aneurysm growth (Table 6.1-25). Review of core laboratory measurements at first follow-up (relative to the location of actual graft placement) suggests graft undersizing.
[i]Patient 1040044 – The patient was treated at the time of the index procedure with a single proximal component. The patient also had aneurysm growth (Table 6.1- 25) and CEC-confirmed migration (Table 6.1-27) and underwent a secondary intervention beyond 2 years (ancillary component placement 798 days post-procedure for the site-reported reasons of distal Type I endoleak and device migration). Review of core laboratory measurements at first follow-up (relative to the location of the actual graft placement) suggests graft undersizing.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Table 6.1-31. Types of secondary interventions

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

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

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

Gender Subset Analysis

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

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

Summary

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

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

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

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

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

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

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

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

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

6.2. Clinical Study for the BTAI Indication

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

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

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

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

Table 6.2-1. Study follow-up schedule

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

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

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

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

Table 6.2-2. Follow-up availability

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

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

Demographics and Patient Characteristics

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

Table 6.2-3. Demographics and patient characteristics

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

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

Table 6.2-4. Pre-existing comorbid medical conditions

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

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

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

Table 6.2-5. Pre-procedure risk

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

Concomitant injuries are presented in Table 6.2-6.

Table 6.2-6. Concomitant injuries

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

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

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

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

Table 6.2-7. Etiology of the thoracic injury

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

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

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

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

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

Table 6.2-9 reports presenting anatomical dimensions.

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

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

Procedural Information

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

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

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

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

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

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

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

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

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

Clinical Utility Measures

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

Table 6.2-12. Clinical utility measures

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

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

Devices Implanted

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Safety Results

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

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

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

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

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

Adverse Events

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

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

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

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

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

Effectiveness Results

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

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

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

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

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

Device Performance

The extent of injury healing, as determined by maximum transverse diameter at the site of injury, observed from the pre-procedure measurement to the 30-day, 6-month, and 12-month follow-up exams (based on core laboratory evaluation), is presented in Table 6.2-20. There were two patients (both at 6 months) who had an increase in diameter

> 5 mm at the site of injury when compared to the pre-procedure measurement, which was associated with endoleak in one patient that required secondary intervention followed by conversion to open surgical repair in the setting of graft undersizing. There were no reports of endoleak or secondary intervention in the other patient, nor was there any change in size (< 5 mm change) when compared to the measurement at first follow-up.

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

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

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

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

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

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

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

Type	Percent Patients(number/total number)		
	30-day[a]	6-month	12-month
Any (new only)	7.1% (3/42)	0	0
Any (new and persistent)	7.1% (3/42)	2.9% (1/34)	0
Multiple	0	0	0
Proximal Type I	0	0	0
Distal Type I	0	0	0
Type II	2.4% (1/42)[b]	0	0
Type III	0	0	0
Type IV	0	0	0
Unknown	4.8% (2/42)[c,d]	2.9% (1/34)[d]	0

[a]Endoleak was not assessed for 1 patient (1200012) due to a suboptimal exam submission (noncontrast exam).

[b]Patient 1200061

[c]Patient 1200035
[d]Patient 1200033 – Patient underwent secondary intervention as described further in Table 6.2-23.

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

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

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

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

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

Tables 6.2-23 and 6.2-24 summarize the site-reported reasons for secondary intervention and types of secondary intervention, respectively. One patient underwent placement of screws for Type I endoleak. One patient underwent balloon angioplasty for device compression. Four patients underwent secondary interventions involving additional stent-graft placement (one to treat dissection, one to treat a pseudoaneurysm, one to treat an area of residual injury or possible endoleak, and one to treat an area of thrombus).

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

Reason	0-30 Days	31-365 Days	366-730 Days
Device compression	0	1[b]	0

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

[a]Patient 1200033 – The patient was treated for a proximal Type I endoleak (per site assessment; core laboratory reported an unknown type of endoleak) 30 days post-procedure; the graft appeared undersized based on core laboratory-assessed aortic diameter measurements. Six Heli-FX™ screws were placed but the endoleak persisted and the secondary intervention was deemed unsuccessful. The patient later underwent conversion to open surgical repair 181 days after the index procedure. The patient survived the surgery and has not experienced any adverse events subsequent to the conversion as of 212 days post-procedure.
[b]Patient 1200012 underwent balloon angioplasty 335 days post-procedure to correct device compression of the proximal section of the second component (with no associated adverse sequelae) noted on the 1-month CT scan (refer to additional details in Table 6.2-22). The secondary intervention was deemed successful.
[c]Patient 1200024 underwent two secondary interventions following the index procedure. An unsuccessful secondary intervention (stent-graft placement) was attempted to treat a pseudoaneurysm proximal to the previously placed stent-graft (counted as a Vascular event in Table 6.2-18) on post-procedure day 74. On post-procedure day 79, the patient underwent a mini-sternotomy, aortic arch debranching, aortic bypass to the innominate and left carotid arteries with Hemashield™ graft, placement of a commercially available endograft, and bilateral chest tube placement to successfully treat the pseudoaneurysm. As described previously, the patient subsequently died on post-operative day 116. The death was adjudicated as procedure-related by the CEC (cause of death was exsanguination due to aortoesophageal fistula).
[d]Patient 1200006 underwent placement of a commercially available stent-graft 219 days post-procedure to treat an area of residual injury or possible endoleak (counted as a Miscellaneous/Other event in Table 6.2-18). The injury was incompletely treated during the index procedure due to the device having been placed too far distally (noted on the 6- month CT scan). The patient also required a left subclavian artery bypass. The secondary intervention was deemed successful.
[e]Patient 1200036 was diagnosed with an aortic dissection distal to the previously placed stent-graft (counted as a Vascular event in Table6.2-18) on post-operative day 286 after returning to the hospital for chest pain. The site noted that the patient was hypertensive and had stopped taking his blood pressure medication. An additional stent graft was placed the following day, which resolved the patient's symptoms. The patient was discharged 2 days after the reintervention.
[f]Patient 1200060 required placement of an additional stent-graft (overlapped with the existing graft) 435 days post-procedure to treat thrombus in the distal stent-graft and native aorta that was noted on the 12-month CT scan (counted as a Miscellaneous/Other event in Table 6.2-18). The site reported that the intervention was successful.

Table 6.2-24. Types of secondary interventions

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

Type*	0-30 Days	31-365 Days	366 – 730 Days
Surgical			
Conversion to open repair	0	0	0
Other	1[a]	2[c,d]	0
Other	0	0	0

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

Longer-term Follow-up

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

Summary

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

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

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

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

6.3. Summary of Supplemental Clinical Information

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

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

6.3.2. Continued Access – Aneurysm/Ulcer Indication

The results from patients treated during the continued access investigation of the aneurysm/ulcer indication (n = 18) were consistent with the results described for the pivotal study cohort, including one patient with aneurysm growth and Type I endoleak (at 6 months) that was associated with graft undersizing following initial treatment of the aneurysm with only a proximal component. Additionally, a portion of the patients

enrolled in the continued access investigation (n = 11) were treated with the rotation handle version of the introduction system, which successfully deployed the stent-graft in all cases, consistent with the deployment results based on bench testing.

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

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

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

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

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

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