Annual Clinical Update

Abstract

Cook is pleased to provide you with this clinical update on the Zenith® Fenestrated AAA Endovascular Graft, which was commercially approved by FDA on April 4, 2012. **Section I** provides an update on results from the long-term post-approval study for the Zenith® Fenestrated AAA Endovascular Graft as of February 1, 2019. The long-term study consists of 88 patients total, including patients enrolled premarket (67) and patients enrolled postmarket (21), with enrollment now complete. Follow-up through 5 years is ongoing. Survival from aneurysm-related mortality at 60 months is 97.5% thus far. To date, no death was found to be related to failure of a component of the device. Newly reported since the previous clinical update is one rupture in the setting of Type III endoleak caused by device separation. There have been no conversions to open surgical repair. Freedom from major morbidity at 60 months is 95.5% thus far. Since the previous clinical update, there has been one new Type I distal endoleak and one new Type III endoleak (same patient noted above with component separation and rupture) based on core laboratory analysis. Seven patients experienced an increase in aneurysm size, one in conjunction with a Type III endoleak, one in conjunction with a distal Type I and Type II (IMA) endoleak, and the rest in conjunction with a Type II endoleak (the origin of the endoleak was the inferior mesenteric artery (IMA) and lumbar artery in 1 patient, the lumbar artery in 2 patients, and the IMA in 1 patient; the origin was not further specified in 1 patient). There have been 2 reports of migration, both in patients with evidence of disease progression at follow-up (without aneurysm pressurization); one patient had associated fenestration stent compression requiring secondary intervention. Three patients were noted to have fracture of a fenestration stent. The first patient was noted to have fracture of a fenestration stent and the seal stent on the Zenith® Fenestrated AAA Endovascular Graft, neither of which resulted in endoleak, clinical renal event, or the need for secondary intervention. This patient also exhibited disease progression at follow-up in the absence of aneurysm pressurization. The second patient with a fenestration stent fracture also did not have endoleak, clinical renal event, or the need for secondary intervention associated with the stent fracture. The third patient with fenestration stent fracture was found to also have renal artery occlusion but did not require reintervention for the occlusion. Approximately half of the patients who underwent reintervention following treatment with the Zenith® Fenestrated AAA Endovascular Graft (11 of 24) did so for renal artery or device stenosis. **Section II** summarizes commercial experience. A total of 16,046 components have been sold in the US since April 4, 2012. A total of 4,224 components have been sold in the same time outside the US (OUS) – note: there are minor differences between Fenestrated devices

available in the US and OUS (e.g., difference in graft diameter, number and location of stents relative to the graft material). There have been 149 reportable complaints recorded during this time. **Section III** summarizes the findings from explant analysis. To date, one explant has undergone analysis. **Section IV** is reserved for any new notes or general instructions to clinicians, of which there are none at this time beyond those already covered as part of the indications, warnings, and precautions from the Instructions for Use (IFU). **Section V** provides a brief summary of the indications, warnings, and precautions from the IFU.

Device Description

The Zenith® Fenestrated AAA Endovascular Graft is a modular system consisting of three components, a proximal body graft, a distal bifurcated body graft, and one iliac leg. The graft modules are constructed of full-thickness woven polyester fabric sewn to self-expanding stainless steel Cook-Z® stents with braided polyester and monofilament polypropylene suture. These materials are identical to the materials used to construct the standard Zenith Flex® AAA Endovascular Graft, with the Zenith® Fenestrated AAA Endovascular Graft also having a nitinol wire ring around the small graft fenestrations.

Unlike the standard Zenith Flex® AAA Endovascular Graft, the Zenith® Fenestrated AAA Endovascular Graft has fenestrations or scallops in the graft material, which allow the proximal edge of the graft material to be placed above the renal arteries while still permitting blood flow to vessels accommodated by the fenestrations or scallops. In order to account for anatomical variation, each proximal body graft is made to order for a specific patient. Ancillary endovascular components (proximal body extensions and distal leg extensions) are also available. Please refer to the IFU for a more detailed description of the components and the delivery system, as well as the indications, warnings, and precautions (also summarized in Section V).

Introduction

One of the conditions of approval of the Zenith® Fenestrated AAA Endovascular Graft was to provide a clinical update to physician users annually. This update has been formatted in accordance with a template that was agreed upon by FDA, industry, and clinicians during a meeting at FDA in October 2008. Accordingly, the clinical update comprises the following sections: Clinical Study Experience (Section I); Worldwide Commercial Experience (Section II); Explant Analysis (Section III); Notes to Clinicians (Section IV); and Brief Summary of Indications, Warnings, and Precautions from IFU (Section V).

Table of Contents

Section I – Clinical Study Experience

Description of Study

The long-term follow-up study is a prospective, observational, single-arm study to evaluate the primary endpoint of 5-year aneurysm-related mortality in patients with aortic or aortoiliac aneurysms who were treated with the Zenith® Fenestrated AAA Endovascular Graft. Additional study endpoints include rupture, conversion, morbidity, device integrity, device patency, changes in aneurysm size, endoleak, migration, and secondary interventions. The study also evaluated training plan effectiveness, as measured by the composite freedom from the following events at 30 days in up to the first 3 postmarket patients from each site: technical failure, loss of patency, rupture, secondary intervention, conversion, and Type I or III endoleak. The long-term study cohort consists of 88 total patients, including patients enrolled premarket (67) as well as patients enrolled postmarket (21). This update reflects data received as of February 1, 2019.

Patient Availability

Patient availability for study follow-up is summarized in Table 1.

Table 1: Follow-up Availability

Follow-up Visit	Patients Eligible for Follow-up[c]	Percent of Data Available[a]			Adequate Imaging to Assess the Parameter[b]				Events Occurring Before Next Interval				
		Clinical	CT	KUB (device X-ray)	Size Increase	Endoleak	Migration	Fracture	Death	Conversion	Lost to Follow-up (LTF) or Withdrawal	Refused Consent for 3-5 Year Follow-up[d]	Not Due for Next Visit
Pre-discharge	88 (0)	100% (88/88)	76.1% (67/88)	78.4% (69/88)	N/A[e]	69.3% (61/88)	N/A[e]	84.1% (74/88)	1	0	0	N/A	0
30-day	87 (0)	98.9% (86/87)	96.6% (84[g]/87)	74.7% (65[g]/87)	73.6% (64/87)	86.2% (75/87)	94.3% (82/87)	94.3% (82/87)	2	0	2	N/A	0
6-month	83 (0)	96.4% (80/83)	94.0% (78/83)	78.3% (65/83)	91.6% (76/83)	84.3% (70/83)	90.4% (75/83)	92.8% (77/83)	1	0	2	N/A	0
12-month	80 (0)	95.0% (76/80)	93.8% (75/80)	71.3% (57/80)	88.8% (71/80)	78.8% (63/80)	90.0% (72/80)	90.0% (72/80)	2	0	2	N/A	0
24-month	76 (0)	92.1% (70/76)	93.4% (71/76)	68.4% (52/76)	84.2% (64/76)	72.4% (55/76)	84.2% (64/76)	89.5% (68/76)	4	0	3	6	0
36-month	63 (0)	93.7% (59/63)	93.7% (59/63)	61.9% (39/63)	85.7% (54/63)	74.6% (47/63)	88.9% (56/63)	90.5% (57/63)	0	0	2	N/A	1
48-month	60 (5)	83.3% (50/60)	80.0% (48/60)	61.7% (37/60)	76.7% (46/60)	56.7% (34/60)	75.0% (45/60)	81.7% (49/60)	0	0	5	N/A	9
60-month	46 (1)	91.3% (42/46)	89.1% (41/46)	73.9% (34/46)	82.6% (38/46)	60.9% (28/46)	80.4% (37/46)	84.8% (39/46)	0	0	1[f]	N/A	N/A

[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] Number in parentheses indicates the number of patients without submitted data who are still eligible for follow-up.
[d] Initial cohort of 30 patients consented only for 2-year follow-up and therefore were asked to reconsent for 3 through 5-year follow-ups.
[e] Pre-discharge represents baseline for comparison at subsequent time points.
[f] One patient (0911120) was withdrawn on POD 2029, outside of the 5-year window.
[g] Due to an error in how a case report form was completed, the missed exams for one patient were included in the numerator and have since been corrected, decreasing the count by 1.

AAA-Related Mortality

AAA-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 independent clinical events committee (CEC).

Figure 1 and Table 2 show the Kaplan-Meier estimates for survival from aneurysm-related mortality. To date, no death was found to be related to failure of a component of the device.

Figure 1: Freedom from AAA-Related Mortality

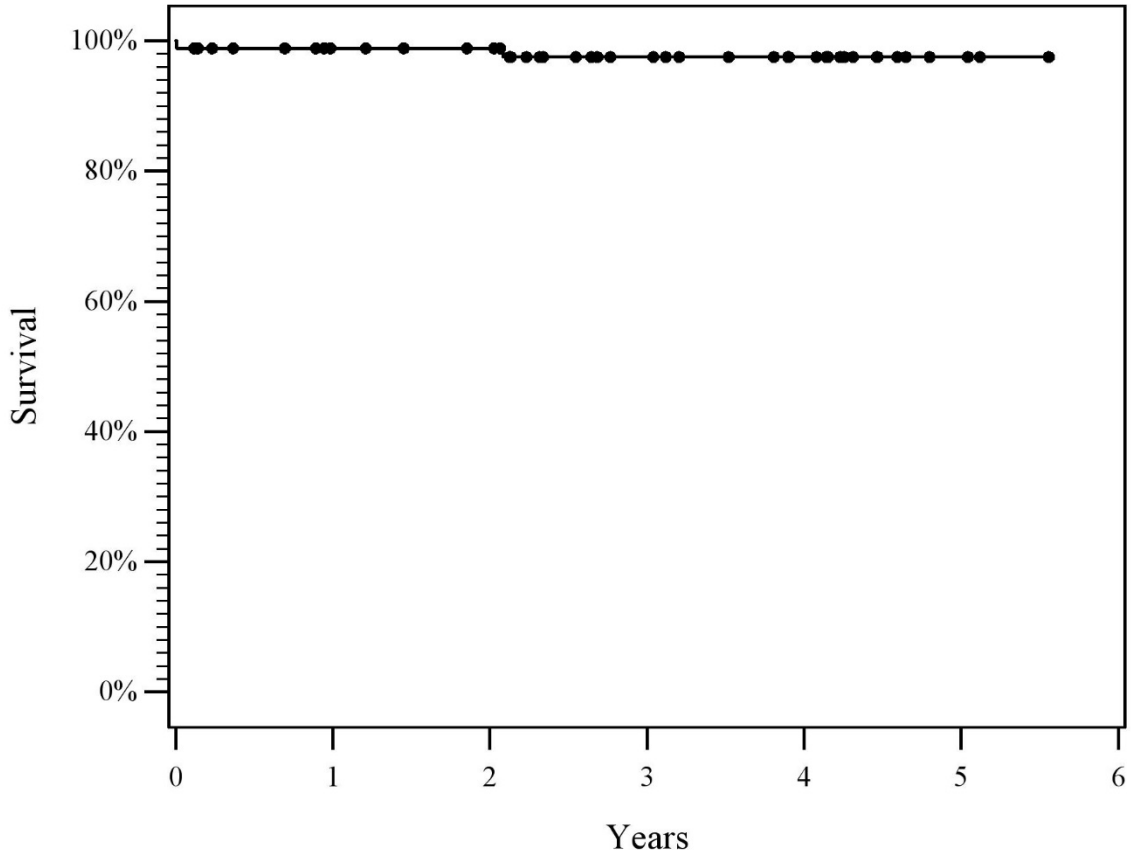

Table 2: Kaplan-Meier AAA-Related Mortality Survival Estimates

Parameter	30 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Kaplan-Meier estimate	98.9%	98.9%	98.9%	97.5%	97.5%	97.5%
Standard error	1.1%	1.1%	1.1%	1.8%	1.8%	1.8%
Cumulative events	1[a]	1	1	2[b]	2	2
Cumulative censored	0	8	11	22	30	41
Number at risk	87	79	76	64	56	45

[a] Patient 0911108: Bowel ischemia on postoperative day (POD) 0 and death on POD 2; CEC adjudicated death as AAA-related (procedure-related).

[b] Patient 0111010: Death on POD 761 according to social security index. Cause of death was unknown; therefore, the CEC was unable to adjudicate, but death was conservatively counted as AAA-related for purpose of Kaplan-Meier analysis.

All-Cause Mortality

Figure 2 and Table 3 show the Kaplan-Meier estimates for freedom from all-cause mortality.

Figure 2: Freedom from All-Cause Mortality

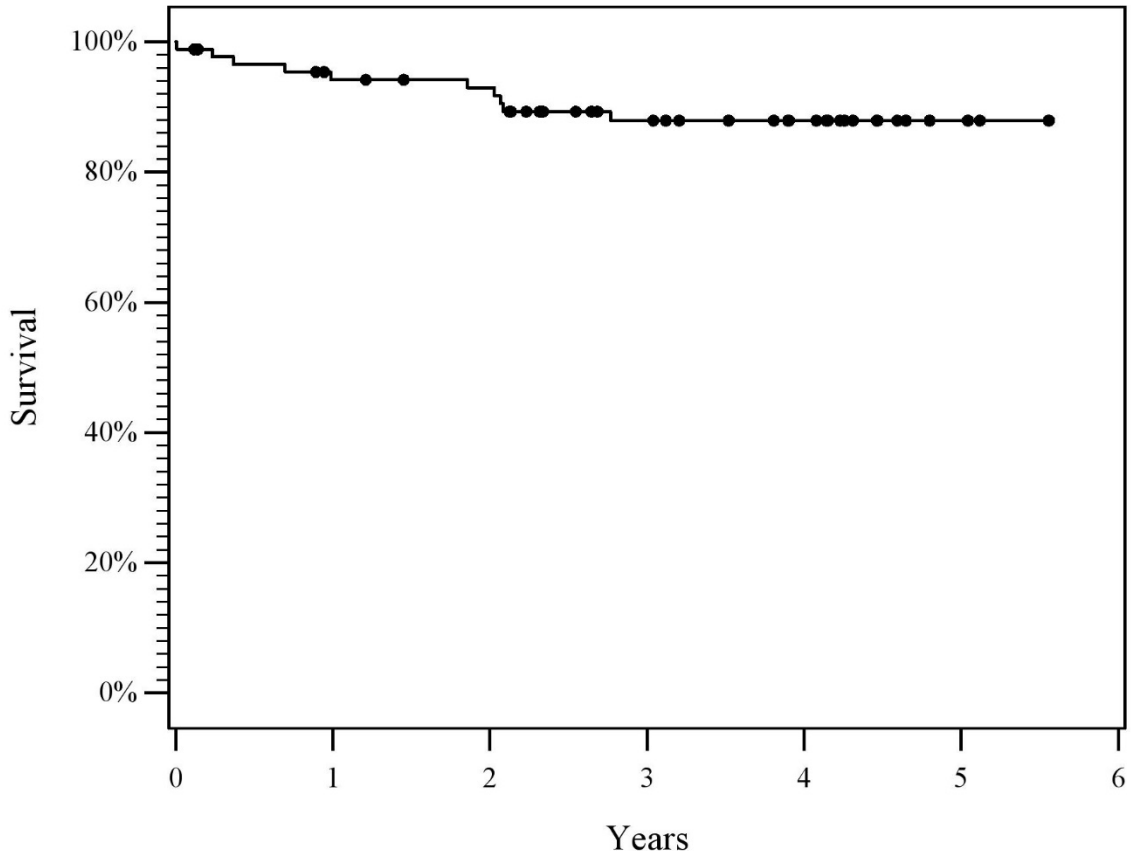

Table 3: Kaplan-Meier All-Cause Mortality Survival Estimates

Parameter	30 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Kaplan-Meier estimate	98.9%	94.2%	93.0%	87.9%	87.9%	87.9%
Standard error	1.1%	2.6%	2.8%	3.8%	3.8%	3.8%
Cumulative events	1	5	6	10	10	10
Cumulative censored	0	4	6	14	22	33
Number at risk	87	79	76	64	56	45

Rupture

Figure 3 and Table 4 show the Kaplan-Meier estimates for freedom from rupture. One rupture was reported since the previous clinical update.

Figure 3: Freedom from Rupture

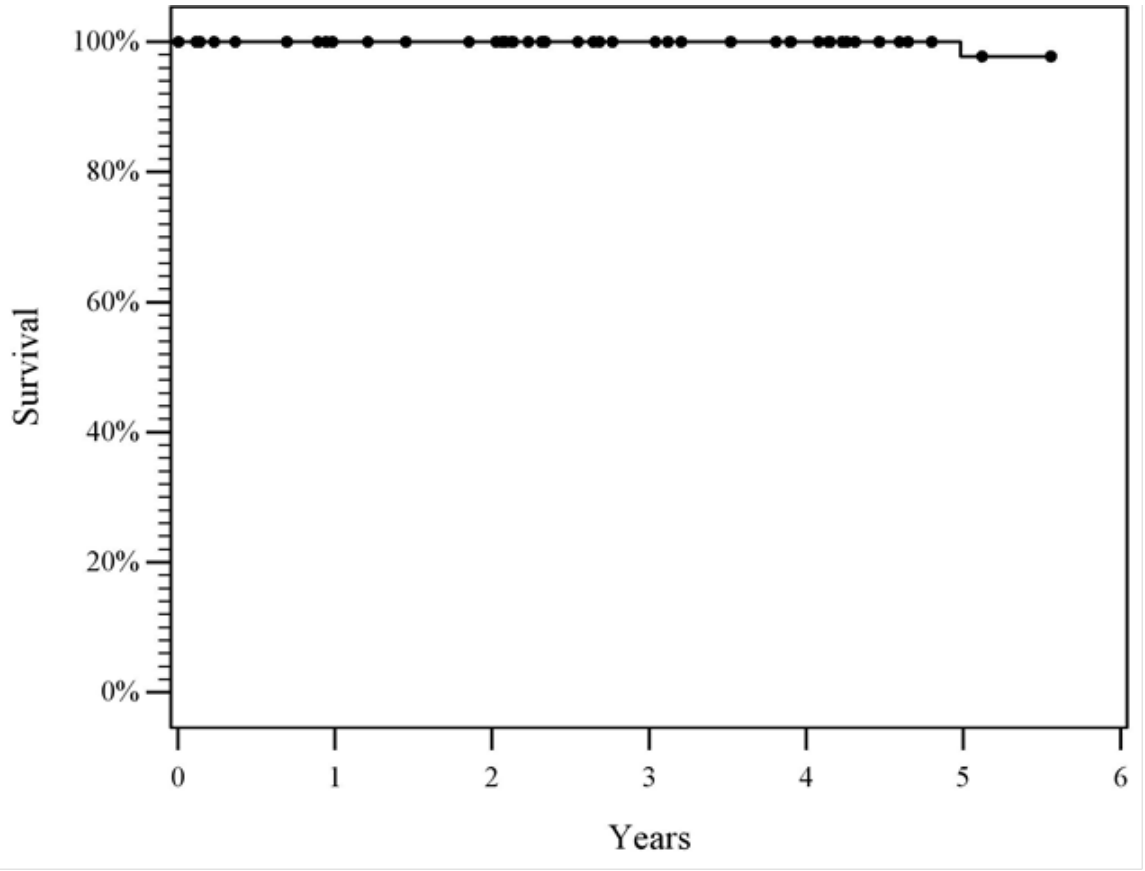

Table 4: Kaplan-Meier Freedom from Rupture Estimates

Parameter	30 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Kaplan-Meier estimate	100%	100%	100%	100%	100%	97.8%
Standard error	0%	0%	0%	0%	0%	2.2%
Cumulative events	0	0	0	0	0	1[a]
Cumulative censored	1	9	12	24	32	43
Number at risk	87	79	76	64	56	44

[a] Patient 1350028.

Patient 1350028 experienced component separation and aneurysm rupture at the 5-year time point. The patient had no prior report of aneurysm growth > 5 mm from the smallest prior measurement and had no prior report of endoleak. The patient was admitted to a nonstudy hospital 1818 days post-procedure after a fall. Abdominal pain and anemia were noted. At 1822 days post-procedure, the 5-year follow-up CT scan was performed, which showed aneurysm growth > 5 mm from baseline. The patient was transferred to the study hospital. The site reported a Type III endoleak between the proximal and distal components of the main body, as well as separation of these components, and aneurysm leak/rupture. The site noted that the endoleak had developed from elongation of the aorta. The core laboratory review also noted a Type III endoleak

and component separation between the proximal and distal components of the main body graft. On the same day, a secondary intervention for aneurysm rupture and device separation was performed, which involved placement of Gore excluder AAA endoprosthesis cuffs. After assessment of a post-secondary intervention CT scan, the site reported successful repair of the endoleak. Core laboratory evaluation of this CT scan is not yet available. Subsequent to the data lock for this clinical update, the CEC adjudicated this event as aneurysm-related (related to component failure). Refer to Section IV for further discussion of this event.

Conversion

There have been no reports of conversion to open surgical repair at any time point.

Major Morbidity

Figure 4 and Table 5 show the Kaplan-Meier estimates for freedom from major morbidity (Q-wave MI, bowel ischemia, paralysis, stroke, reintubation, renal failure requiring dialysis). Events determined by the CEC to be related to a preexisting condition are not included. No new events have been reported after 30 days.

Figure 4: Freedom from Major Morbidity

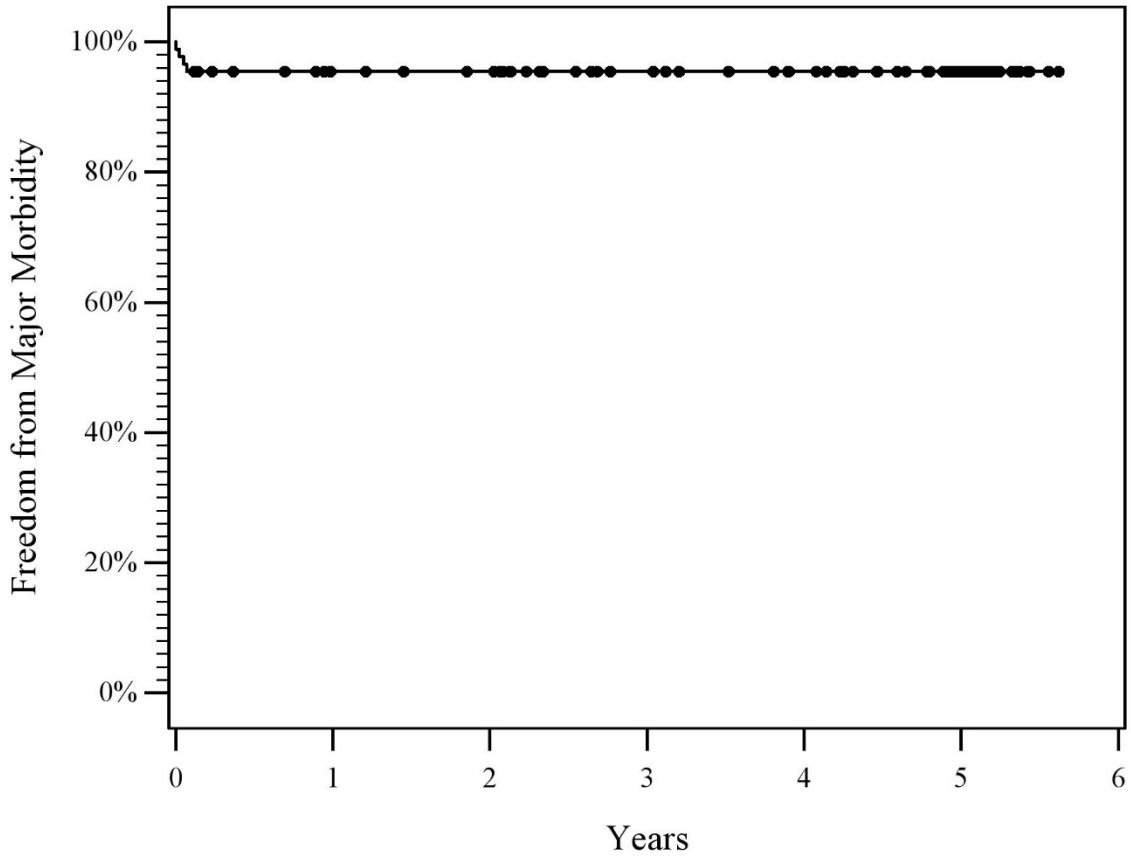

Table 5: Kaplan-Meier Estimates for Freedom from Major Morbidity

Event	Parameter	30 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Major morbidity (any)	Kaplan-Meier estimate	95.5%	95.5%	95.5%	95.5%	95.5%	95.5%
	Standard error	2.2%	2.2%	2.2%	2.2%	2.2%	2.2%
	Cumulative events	4	4	4	4	4	4
	Cumulative censored	0	8	11	23	31	53
	Number at risk	84	76	73	61	53	31
Q-wave MI	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%
	Cumulative events	0	0	0	0	0	0
	Cumulative censored	1	9	12	24	32	56
	Number at risk	87	79	76	64	56	32
Bowel ischemia	Kaplan-Meier estimate	96.6%	96.6%	96.6%	96.6%	96.6%	96.6%
	Standard error	1.9%	1.9%	1.9%	1.9%	1.9%	1.9%
	Cumulative events	3[a,b,c]	3	3	3	3	3
	Cumulative censored	0	8	11	23	31	54
	Number at risk	85	77	74	62	54	31
Spinal cord ischemia/ paralysis	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%
	Cumulative events	0	0	0	0	0	0
	Cumulative censored	1	9	12	24	32	56
	Number at risk	87	79	76	64	56	32

Event	Parameter	30 Days	365 Days	730 Days	1095 Days	1460 Days	1825 Days
Stroke	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%
	Cumulative events	0	0	0	0	0	0
	Cumulative censored	1	9	12	24	32	56
	Number at risk	87	79	76	64	56	32
Reintubation	Kaplan-Meier estimate	100%	100%	100%	100%	100%	100%
	Standard error	0%	0%	0%	0%	0%	0%
	Cumulative events	0	0	0	0	0	0
	Cumulative censored	1	9	12	24	32	56
	Number at risk	87	79	76	64	56	32
Renal failure requiring dialysis	Kaplan-Meier estimate	98.9%	98.9%	98.9%	98.9%	98.9%	98.9%
	Standard error	1.1%	1.1%	1.1%	1.1%	1.1%	1.1%
	Cumulative events	1[d]	1	1	1	1	1
	Cumulative censored	1	9	12	24	32	55
	Number at risk	86	78	75	63	55	32

[a] Patient 0211011: Bowel ischemia on POD 25; recovered following treatment with IV fluids and antibiotics.
[b] Patient 0911108: Bowel ischemia on POD 0 and death on POD 2.
[c] Patient 1111102: Bowel ischemia on POD 8; recovered following treatment with antibiotics.
[d] Patient 1350027: Renal failure requiring dialysis on POD 18. The site later indicated that the patient was on medical management and previously received one treatment of dialysis (AE still considered to be unresolved).

Device Integrity

The percentage of patients with device integrity findings at each follow-up time point based on the results of core laboratory analysis is presented in Table 6. As indicated in the footnotes to the table, isolated observations of device integrity findings have been noted, where the need for associated reintervention was infrequent. There has been one report of component separation since the previous clinical update.

Table 6: Percent of Patients with Device Integrity Findings Based on Core Laboratory Analysis (Date of First Occurrence)

Finding	Post-procedure	1-month	6-month	12-month	24-month	36-month	48-month	60-month	Total Number of Patients
Stent-graft									
Barb separation	0% (0/74)	0% (0/82)	1.3% (1/77)[a]	1.4% (1/72)[b]	1.5% (1/68)[c]	0% (0/57)	2.0% (1/49)[m]	2.6% (1/39)[n]	5
Stent fracture (single)	0% (0/74)	0% (0/82)	0% (0/77)	2.8% (2/72)[d,j]	0% (0/68)	0% (0/57)	0% (0/49)	0% (0/39)	2
Stent fracture (multiple)	0% (0/74)	0% (0/82)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/57)	0% (0/49)	0% (0/39)	0
Component separation	0% (0/74)	0% (0/82)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/57)	0% (0/49)	2.6% (1/39)[o]	1
Limb separation	0% (0/74)	0% (0/82)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/57)	0% (0/49)	0% (0/39)	0
Stent-to-graft separation	0% (0/74)	0% (0/82)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/57)	0% (0/49)	0% (0/39)	0
Other	0% (0/74)	0% (0/82)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/57)	0% (0/49)	0% (0/39)	0
Fenestration stent									
Fracture	0% (0/74)	0% (0/83)	2.6% (2/77)[e,k]	1.4% (1/72)[d]	0% (0/68)	0% (0/58)	0% (0/47)	0% (0/39)	3
Separation	0% (0/74)	0% (0/83)	0% (0/77)	0% (0/72)	0% (0/68)	0% (0/58)	0% (0/47)	0% (0/39)	0
Other	0% (0/74)	0% (0/83)	3.9% (3/77)[f,g,h]	1.4% (1/72)[i]	0% (0/68)	1.7% (1/58)[l]	0% (0/47)	0% (0/39)	5

Note: Grey shading indicates 0 device integrity findings.

[a] Patient 0421003: Separation of a single fixation barb. No clinical sequelae related to the barb separation were reported.

[b] Patient 0111009: Separation of a single fixation barb. No clinical sequelae related to the barb separation were reported.

[c] Patient 0511008: Separation of two barbs. No clinical sequelae related to the barb separation were reported, although radiographic migration (approximately 10 mm over 5 years) was observed and was likely due to longitudinal progression of disease with further aortic neck dilatation.

[d] Patient 0411001: Fracture of sealing stent (at the distal edge of the scallop fenestration) and left renal fenestration stent (uncovered, balloon-expandable 316L stainless steel biliary/iliac stent), but in a patient with progressive aneurysmal disease within and proximal to the treated segment, which likely resulted in uncharacteristic tension/loading of the stents. No subsequent renal events, endoleak, or secondary interventions were reported in this patient.

[e] Patient 0511010: Fracture of left renal fenestration stent (Zenith® Alignment Stent) not readily confirmed based on subsequent bench top CT imaging studies that showed the same appearance of fracture, but in an entirely intact stent.

[f] Patient 1111011: Deformation of right renal fenestration stent (Zenith® Alignment Stent) with no measurable graft movement > 5 mm. On POD 398, a secondary intervention was performed to treat worsening renal function and an angiogram was performed to attempt to cannulate the right renal artery; cannulation was unsuccessful. On POD 435, the patient had a hepatic artery to right renal artery bypass using reverse greater saphenous vein to treat an occlusion caused by the crushed right renal stent. This secondary intervention was successful.

[g] Patient 0511003: Slight compression of left renal fenestration stent (uncovered, balloon-expandable 316L stainless steel biliary stent) with no measurable graft movement > 5 mm. Due to stenosis, on POD 1539, the patient underwent angioplasty and stent placement. Restenosis was identified at the 60-month follow-up and a successful secondary intervention was performed on POD 1876. The CEC adjudicated this event as unrelated.

[h] Patient 0511007: Slight compression of the left renal fenestration stent (uncovered, balloon-expandable 316L stainless steel biliary stent) with no measurable graft movement > 5 mm and not requiring secondary intervention.

[i] Patient 0511006: Compression of the right renal fenestration stent (uncovered, balloon-expandable 316L stainless steel biliary stent) associated with graft migration (approximately 12 mm by 24 months) due likely to longitudinal progression of disease with further aortic neck dilatation. Due to stenosis, on POD 883, the patient underwent angioplasty and stent placement.
[j] Patient 0611101: Single stent fracture in the proximal graft, approximately at the level of the renal arteries, was observed on the 12-month KUB. No clinical sequelae related to the stent fracture were reported.
[k] Patient 0211103: Fracture and deformity of the left renal fenestration stent (Zenith® Alignment Stent). On POD 1124, the patient was reported to have an occlusion of a fenestrated renal vessel, but the occlusion was not treated (secondary intervention for stenosis on the right side was performed on POD 1582). The patient was noted to have creatinine rise > 2.0 mg/dl and > 30% above baseline during two follow-up periods. The CEC adjudicated this event as AAA-related (procedure-related and device-related due to progression of the left renal artery stenosis to occlusion).
[l] Patient 1111102: Compression of left renal stent due to angulation. No other renal events were reported, and the patient did not require a secondary intervention for this event.
[m] Patient 0111017: Separation of one barb at 48 months. Barb separation was confirmed by the CEC, noted for the first time at 24 months following retrospective review of imaging.
[n] Patient 1111013: Separation of one barb observed at 60 months. Barb separation was confirmed by the CEC. No clinical sequelae related to the barb separation were reported.
[o] Patient 1350028: Component separation of the proximal and distal main body grafts. The patient also had growth > 5 mm, Type III endoleak, and rupture. On POD 1822, the patient underwent successful endovascular repair.

Patency

The percentage of patients with patency loss involving either the stent-graft or a vessel accommodated by a fenestration is provided in Table 7. There were no new reports of patency loss since the previous clinical update.

Table 7: Percent of Patients with Loss of Patency Based on Core Laboratory Analysis or as Reported by the Site (Date of First Occurrence)

Post-procedure	1-month	6-month	12-month	24-month	36-month	48-month	60-month
0% (0/67)	0% (0/82)	2.6% (2/78)[a,b]	2.7% (2/74)[c,d]	0% (0/66)	1.8% (1/56)[e]	0% (0/44)	0% (0/37)

[a] Patient 0211008 had renal artery occlusion; the patient underwent secondary intervention, as described in Table 11.
[b] Patient 0911115 had accessory renal artery occlusion; no secondary intervention was performed.
[c] Patient 0611003 had renal artery occlusion; no secondary intervention was performed.
[d] Patient 1111011 had renal artery occlusion; the patient underwent secondary intervention, as described in Table 11.
[e] Patient 0211103 had renal artery occlusion and fenestration stent fracture. This patient had serum creatinine rise > 2.0 mg/dl and > 30% above baseline during two follow-up periods; no secondary intervention was performed for left renal occlusion.

Change in Aneurysm Size

Table 8 reports the percentage of patients with an increase (> 5 mm), decrease (> 5 mm), or no change (≤ 5 mm) in aneurysm diameter based on core laboratory analysis at each follow-up time point subsequent to pre-discharge, which represents baseline. Any patient with size increase and associated endoleak and/or requiring a secondary intervention is indicated by a footnote. There has been one new patient with aneurysm size increase since the previous clinical update.

Table 8: Percent of Patients with an Increase, Decrease, or No Change in Aneurysm Size Based on Core Laboratory Analysis

Item	1-month	6-month	12-month	24-month	36-month	48-month	60-month
Increase (> 5 mm)	0% (0/64)	0% (0/76)	1.4% (1/71)[e]	1.6% (1/64)[f,g]	7.4% (4/54)[a,b,d,f]	8.7% (4/46)[b,c,d,f]	5.3% (2/38)[d,h]
Decrease (> 5 mm)	1.6% (1/64)	52.6% (40/76)	66.2% (47/71)	70.3% (45/64)	74.1% (40/54)	76.1% (35/46)	76.3% (29/38)
No change (≤ 5 mm)	98.4% (63/64)	47.4% (36/76)	32.4% (23/71)	28.1% (18/64)	18.5% (10/54)	15.2% (7/46)	18.4% (7/38)

[a] Patient 0511004 had persistent Type II endoleak requiring secondary intervention on POD 1393, with no additional growth as of the 5-year follow-up.
[b] Patient 0111016 had a persistent Type II endoleak reported at the 3-year and 4-year visits. A secondary intervention (coil embolization) was performed on POD 1490.
[c] Patient 0211010 had a persistent Type II endoleak requiring secondary intervention on POD 239, but the endoleak was still evident at the 48-month follow-up visit. The patient was not assessed for endoleak at the 5-year follow-up visit.
[d] Patient 0211011 had a persistent Type II endoleak at the 3, 4, and 5-year visits. A secondary intervention (coil embolization and ancillary component placement) was performed on POD 1746.
[e] Patient 1350039 had a site-reported persistent Type II endoleak at the 1-year visit. The core laboratory reported that endoleak could not be assessed.
[f] Patient 1350008 had a persistent Type II endoleak at the 2-year and 3-year visits.
[g] Patient 1350031 was previously reported to have a persistent Type II endoleak at the 2-year visit. A secondary intervention (coil embolization) was performed on POD 763. Since the previous clinical update, the core laboratory received the 3-year CT scan for this patient and concurrently amended the baseline aneurysm diameter measurement to be a larger value. The 2-year aneurysm diameter measurement is now no longer > 5 mm larger than baseline, so the count has decreased by 1.
[h] Patient 1350028 had a Type III endoleak (component separation) at the 5-year visit, resulting in a secondary intervention to treat aneurysm growth and rupture.

Endoleak

Table 9 reports the percentage of patients with endoleak (by type) at each follow-up time point based on the results of core laboratory analysis. One distal Type I and one Type III endoleak were reported since the previous clinical update.

Table 9: Percent of Patients with Endoleak Based on Core Laboratory Analysis

Type	Pre-discharge	1-month	6-month	12-month	24-month	36-month	48-month	60-month	Total Number of Patients
Any (new only)	31.1% (19/61)	6.7% (5/75)	7.1% (5/70)	3.2% (2/63)	1.8% (1/55)	2.1% (1/47)	0% (0/34)	3.6% (1/28)	34
Any (new and persistent)	31.1% (19/61)	24.0% (18/75)	25.7% (18/70)	27.0% (17/63)	25.5% (14/55)	25.5% (12/47)	14.7% (5/34)	10.7% (3/28)	
Multiple	0% (0/61)	0% (0/75)	0% (0/70)	0% (0/63)	0% (0/55)	0% (0/47)	0% (0/34)	0% (0/28)	0
Proximal Type I	0% (0/61)	0% (0/75)	0% (0/70)	0% (0/63)	0% (0/55)	0% (0/47)	0% (0/34)	0% (0/28)	0
Distal Type I	0% (0/61)	0% (0/75)	0% (0/70)	0% (0/63)	0% (0/55)	2.1% (1[b]/47)	0% (0/34)	0% (0/28)	1
Type II	29.5% (18/61)	24.0% (18/75)	22.9% (16/70)	22.2% (14/63)	20.0% (11/55)	21.3% (10/47)	14.7% (5/34)	7.1% (2/28)	30[a]
Type III	0% (0/61)	0% (0/75)	0% (0/70)	0% (0/63)	0% (0/55)	0% (0/47)	0% (0/34)	3.6% (1[c]/28)	1
Type IV	0% (0/61)	0% (0/75)	0% (0/70)	0% (0/63)	0% (0/55)	0% (0/47)	0% (0/34)	0% (0/28)	0
Unknown	1.6% (1/61)	0% (0/75)	2.9% (2/70)	4.8% (3/63)	5.5% (3/55)	2.1% (1/47)	0% (0/34)	0% (0/28)	6[a]

Note: Grey shading indicates 0 endoleaks.

[a] Includes one patient who had a Type II endoleak at pre-discharge and an unknown endoleak type at 6, 12, 24, and 36 months; one patient who had a Type II endoleak at pre-discharge, 1 month, and 6 months, and an unknown endoleak type at 24 months; one patient who had an unknown endoleak type at 12 months and a Type II endoleak at 24 months; and one patient who had a Type II endoleak at 1 month, 12 months, 24 months, and 36 months, and an unknown endoleak type at 6 months.

[b] Patient 1350032: additional details are available in the Secondary Interventions section.

[c] Patient 1350028 experienced component separation. Additional details are available in the Rupture section.

Migration

Table 10 reports the percentage of patients with CEC-confirmed radiographic migration (≥ 10 mm) or clinically significant migration (measurable movement of the stent-graft > 5 mm and development of a Type I endoleak or renal stenosis/occlusion with demonstrable deformation of the mating renal stent based on core laboratory analysis) at each follow-up time point (date of first occurrence). There have been no new reports of migration since the previous clinical update.

Table 10: Percent of Patients with CEC-Confirmed Migration (Date of First Occurrence)

Item	1-month	6-month	12-month	24-month	36-month	48-month	60-month
Radiographic migration	0% (0/82)	0% (0/75)	0% (0/72)	1.6% (1/64)[a]	0% (0/56)	0% (0/45)	2.7% (1/37)[b]
Clinically significant migration	0% (0/82)	0% (0/75)	0% (0/72)	1.6% (1/64)[a]	0% (0/56)	0% (0/45)	0% (0/37)

[a] Patient 0511006 had renal stenosis from associated stent compression (uncovered, balloon-expandable 316L stainless steel biliary stent) requiring secondary intervention. Longitudinal progression of disease with further aortic neck dilatation likely resulted in migration. There were no Type I or Type III endoleaks or increase in aneurysm size in this patient. The total amount of graft movement detected at the time of the clinically significant migration was approximately 12 mm (relative to the celiac artery).
[b] Patient 0511008 was without any associated renal stenosis requiring secondary intervention and additionally did not have any endoleak or increase in aneurysm size. Longitudinal progression of disease with further aortic neck dilatation likely resulted in migration. The total amount of graft movement was approximately 10 mm (relative to the celiac artery), which occurred over 60 months. No interventions were performed for this patient.

Secondary Interventions

Table 11 summarizes the site-reported reasons for and types of secondary interventions. There have been two new patients with reintervention since the previous clinical update.

Table 11: Reasons for and Types of Secondary Intervention (as Reported by the Site)

Reason / Type	0-30 Days	31-365 Days	366-730 Days	731-1095 Days	1096-1460 Days	1461-1825 Days
Aneurysm rupture	0	0	0	1	0	1
Ancillary component	--	--	--	q	--	w
Symptoms	0	0	0	0	0	0
N/A	--	--	--	--	--	--
Device/renal stenosis	1	2	3	3	1	2
Angioplasty/stenting	--	b,c	g,h,i	h,k,o	l	n,t
Other	a	--	--	--	--	--
Device migration	0	0	0	1	0	0
Angioplasty/stenting	--	--	--	h	--	--
Device separation	0	0	0	0	0	1
Ancillary component	--	--	--	--	--	w
Occlusion	0	1	1	0	0	0
Bypass	--	d	j	--	--	--
Device kink	0	0	0	0	0	0
N/A	--	--	--	--	--	--
Infection	0	0	0	0	0	0
N/A	--	--	--	--	--	--

Reason Type	0-30 Days	31-365 Days	366-730 Days	731-1095 Days	1096-1460 Days	1461-1825 Days
Type I proximal	0	0	0	1	2	0
Angioplasty/stenting	--	--	--	p	--	--
Coil embolization	--	--	--	--	p	--
Angiogram/catheterization	--	--	--	--	p	--
Type I distal	0	1	0	0	0	1
Coil embolization	--	u	--	--	--	a
Ancillary component	--	--	--	--	--	a
Type IIA (vessel perfusion)	0	3	0	1	1	1
Coil embolization	--	e,f,u	--	v	--	r
Ligation	--	--	--	--	m	--
Type IIB (vessel perfusion)	0	0	0	0	0	0
N/A	--	--	--	--	--	--
Type III (graft overlap joint)	0	0	0	0	1	1
Ancillary component	--	--	--	--	--	w
Angioplasty/stenting	--	--	--	--	s	--
Type IV (through graft body)	0	0	0	0	0	0
N/A	--	--	--	--	--	--
Unknown type	0	0	0	1	0[s]	0
Ancillary component	--	--	--	q	--	--
Other	0	0	1	1	2	0
Angiogram/catheterization	--	--	j	--	m	--
Angioplasty/stenting	--	--	--	k	--	--
Coil embolization/ancillary component	--	--	--	--	x	--

[a] Patient 0211011: Angiography revealed that the right renal artery was severely stenosed. Attempted cannulation was unsuccessful, as the fenestration stent (Zenith® Alignment Stent) was not flared at the time of the initial implant procedure. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. The CEC adjudicated this event as AAA-related. The site reported a distal Type I endoleak and on POD 1746, the patient underwent successful coil embolization and ancillary component placement.
[b] Patient 0111008: The patient experienced right renal artery stenosis (uncovered, balloon-expandable 316L stainless steel biliary stent). On POD 238, the patient was successfully treated with angioplasty and additional stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. Follow-up demonstrated a patent renal artery. The CEC adjudicated this event as AAA-related.
[c] Patient 0111014: The patient experienced bilateral renal artery stenoses (uncovered, balloon-expandable 316L stainless steel biliary stents). On POD 245, the patient was successfully treated with angioplasty and additional stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. Follow-up demonstrated a patent renal artery. The CEC adjudicated this event as AAA-related.
[d] Patient 0211008: An angiogram demonstrated an occluded left renal artery with proximal compression of the left renal stent (uncovered, balloon-expandable 316L stainless steel biliary/renal stent). On POD 222, the patient was successfully treated with iliorenal bypass. Compression without evidence of migration was likely due to suboptimal deployment of the renal stent into the middle/upper portion of the fenestration. The CEC adjudicated this event as AAA-related.
[e] Patient 0211010: The patient experienced persistent Type II endoleak. On POD 239, the patient was successful treated with coil embolization.
[f] Patient 0611101: The patient experienced Type II endoleak, causing an enlarged AAA. On POD 224, the patient was successfully treated with coil embolization and NBCA glue.
[g] Patient 0211007: The patient experienced right renal artery stenosis (uncovered, balloon-expandable 316L stainless steel biliary/renal stent). On POD 406, the patient was successfully treated with angioplasty and additional stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. The CEC adjudicated this event as AAA-related.
[h] Patient 0111017: Renal ultrasound demonstrated a right renal artery stenosis (Zenith® Alignment Stent). On POD 427, the patient was successfully treated with stent placement. The CEC adjudicated the event as AAA-related. Left renal artery in-stent stenosis (Zenith® Alignment Stent) was noted on POD 840 and the

patient was successfully treated with stent placement. The core laboratory retrospectively noted separation of one barb observed at 48 months. Barb separation was confirmed by the CEC, noted for the first time at 2 years; however, the site determined the stenosis was due to device migration. The CEC adjudicated the stenosis to be AAA-related and due to the site-reported migration (no migration according to the core laboratory).

[i] Patient 1211109: The patient experienced left renal artery stenosis (Zenith® Alignment Stent). On POD 382, the patient was successfully treated with angioplasty and stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. Core laboratory analysis of the procedural angiogram noted a patent graft and stented, patent renal arteries with no evidence of an endoleak. CEC adjudicated this event as AAA-related.

[j] Patient 1111011: An angiogram demonstrated an occluded right renal artery (Zenith® Alignment Stent). On POD 398, a percutaneous attempt to cannulate the right renal artery stent was unsuccessful. On POD 435, the patient, who had a right renal stent that was crushed at the orifice of the vessel, was successfully treated with surgical common hepatic artery to right renal artery bypass performed using reverse greater saphenous vein to treat a crushed right renal stent at the orifice of the vessel. The CEC adjudicated this event as AAA-related.

[k] Patient 0511006: The patient experienced right renal artery stent compression and subsequent stenosis (uncovered, balloon-expandable 316L stainless steel biliary stent). On POD 883, the patient was successfully treated with angioplasty and stent placement. Compression of the fenestration stent associated with graft migration (approximately 12 mm by 24 months) was likely due to longitudinal progression of disease with further aortic neck dilatation. Intra-operative angiogram demonstrated a patent right renal artery at the end of the procedure. The CEC adjudicated this event as AAA-related.

[l] Patient 0511009: The patient experienced bilateral renal artery stenosis (uncovered, balloon-expandable 316L stainless steel biliary stents). On POD 1400, the patient was successfully treated with bilateral angioplasty and stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. The CEC adjudicated this event as AAA-related.

[m] Patient 0511004: The patient underwent diagnostic angiogram for suspected Type IIA and Type III endoleaks, which were not detected on POD 1137. On POD 1393, the patient underwent additional intervention, which involved laparotomy, a suture ligation of the inferior mesenteric artery (IMA), and exploration of the aneurysm sac to successfully remedy the Type II endoleak with aneurysm growth.

[n] Patient 0511003: The patient experienced left renal artery stenosis (uncovered, balloon-expandable 316L stainless steel biliary stent) from slight compression of the fenestration stent (with no measurable graft movement > 5 mm). On POD 1539, the patient was successfully treated with angioplasty and stent placement. The CEC adjudicated this event as AAA-related.

[o] Patient 0611105: The patient experienced right renal artery stenosis (Zenith® Alignment Stent). On POD 743, the patient was successfully treated with angioplasty and stent placement. No evidence of graft migration or stent deformation, suggesting the stenosis may have resulted from local thrombus formation or intimal hyperplasia within the stented segment. The CEC adjudicated this event as AAA-related.

[p] Patient 0911006: Based on the site assessment of the imaging, the 2-year CT scan revealed a proximal Type I endoleak at the junction of the Zenith® Fenestrated AAA Endovascular Graft and the Zenith® Alignment Stent; however, core laboratory analysis noted an endoleak of unknown type. On POD 1003, the patient was successfully treated with balloon-expandable covered stent placement. Based on the site assessment of the imaging, the 3-year CT scan revealed a proximal Type I endoleak; however, the core laboratory analysis noted an endoleak of unknown type. On POD 1100, the attempt at coil embolization of the vessel that supplied the endoleak was not successful, as access to the vessel could not be obtained. On POD 1142, the patient underwent a third, successful secondary intervention involving coil embolization of the vessel thought to be contributing to the observed endoleak.

[q] Patient 1211106: The patient experienced an unknown type endoleak with reported infrarenal aneurysm sac rupture. On POD 1031, the patient underwent successful placement of two additional components in the iliac arteries and bilateral limb dilatation with a CODA balloon. A repeat angiography revealed no endoleak. The core laboratory noted a Type II endoleak, but no aneurysm sac rupture. The CEC adjudicated this event as AAA-related, and stated they did not consider this to be an aneurysm rupture, but rather a new endoleak.

[r] Patient 0111016: The patient experienced a Type II endoleak. On POD 1490, the patient underwent successful coil embolization.

[s] Patient 1411101: The patient experienced an endoleak of an originally unknown type. On POD 1188, the patient underwent successful angioplasty and covered stent placement in the left renal artery. The site later reported this to be a Type III endoleak (reported as Type II by the core laboratory).
[t] Patient 0211103: The patient experienced renal stenosis (Zenith® Alignment Stent). On POD 1582, the patient underwent successful renal angioplasty. The CEC adjudicated this event as AAA-related.
[u] Patient 1350021: The patient experienced distal Type I and Type II endoleaks according to the site. On POD 263, the patient underwent successful coil embolization.
[v] Patient 1350031: The patient experienced a Type II endoleak as reported by the site. On POD 763, the patient underwent successful coil embolization.
[w] Patient 1350028: The patient experienced component separation and aneurysm rupture. On POD 1822, the patient underwent successful endovascular repair. More information is available in the Rupture section.
[x] Patient 1350032: On POD 1316, the patient underwent a successful coil embolization of the left hypogastric artery and placement of a distal extension into the left external iliac artery to treat a distal Type I endoleak of the left iliac leg of the device. The site commented that the study aneurysm had decreased in size, but a left common iliac aneurysm had grown and required treatment. The site noted a Type Ib endoleak. The core laboratory had reported a distal Type I endoleak at the 3-year time point, approximately 6 months prior to the secondary intervention.

Summary

Patient enrollment is complete and patient follow-up is ongoing. Survival from aneurysm-related mortality at 60 months is 97.5% thus far. To date, no death was found to be related to failure of a component of the device. Newly reported since the previous clinical update is one rupture in the setting of Type III endoleak caused by device separation. There have been no conversions to open surgical repair. Freedom from major morbidity at 60 months is 95.5% thus far.

Since the previous clinical update, there has been one new Type I distal endoleak and one new Type III endoleak (same patient noted above with component separation and rupture) based on core laboratory analysis. Seven patients experienced an increase in aneurysm size, one in conjunction with a Type III endoleak, one in conjunction with a distal Type I and Type II (IMA) endoleak, and the rest in conjunction with a Type II endoleak (the origin of the endoleak was the IMA and lumbar artery in 1 patient, the lumbar artery in 2 patients, and the IMA in 1 patient; the origin was not further specified in 1 patient). There have been 2 reports of migration, both in patients with evidence of disease progression at follow-up (without aneurysm pressurization); one patient had associated fenestration stent compression with stenosis requiring secondary intervention. Three patients were noted to have fracture of a fenestration stent. The first patient was noted to have fracture of a fenestration stent as well as the seal stent on the Zenith® Fenestrated AAA Endovascular Graft, but neither fracture resulted in endoleak, clinical renal event, or the need for secondary intervention. This patient also exhibited disease progression at follow-up in the absence of aneurysm pressurization. The second patient with a fenestration stent fracture was identified without endoleak, subsequent clinical renal event, or need for secondary intervention. The third patient with fenestration stent

fracture was found to also have renal artery occlusion, but did not require a secondary intervention for the occlusion.

Approximately half of the patients who underwent reintervention following treatment with the Zenith® Fenestrated AAA Endovascular Graft (11 of 24) did so for renal artery or device stenosis, which was associated with stent compression in 2 patients (one of whom also had graft migration, as noted above). Two patients with renal artery occlusion also underwent secondary intervention; both occlusions were associated with stent compression. Careful patient selection, device planning/sizing, as well as device placement during the initial procedure (e.g., ensuring deployment of the fenestration stent in the lower portion of the graft fenestration) are important to mitigate the potential for reintervention due to stent compression that may result in either renal artery stenosis or occlusion.

Section II – Worldwide Commercial Experience

The Zenith® Fenestrated AAA Endovascular Graft was commercially available in the US soon after marketing approval was granted by FDA on April 4, 2012. The device has been commercially available OUS since 2002 – note: there are some differences between Fenestrated devices available in the US and OUS (e.g., difference in graft diameter at the overlap, number and location of stents relative to the graft material).

Table 12 summarizes the total number of Zenith Fenestrated AAA Endovascular Graft components distributed worldwide between April 4, 2012 and March 31, 2019.

Table 12: Total Number of Zenith® Fenestrated AAA Endovascular Graft Components Sold Between April 4, 2012 and March 31, 2019

Component	Total US Number Sold (subtotal for past year)	Total OUS Number Sold (subtotal for past year)
ZFEN-P (proximal component)	8,476 (1,737)	2,141 (352)
ZFEN-D (distal component)	7,570 (1,475)	2,083 (324)
Total	**16,046 (3,212)**	**4,224 (676)**

William A. Cook Australia Pty Ltd. (WCA) evaluates product performance from this commercial experience based on complaint reporting systems throughout the world. All complaints received related to the Zenith® Fenestrated AAA Endovascular Graft are processed through the Customer Relations Department at William A. Cook Australia Pty Ltd, the manufacturer of the device, during which complaints are assessed for reportability to regulatory authorities and are subject to a quality engineering and, as needed, clinical review. Based on this review, additional information may be requested from the user facility at which the event occurred. The Quality Engineering group makes a final determination of root cause, and the findings are evaluated for any necessary corrective action. Complaint trending is performed as part of each complaint investigation and risk documentation is subsequently reviewed. Additionally, complaint trending is performed monthly and biannually to determine if there are trends in reported complaints requiring action.

The data presented in Table 13 summarizes all reportable complaints (procedural and follow-up) in the US and outside the US for the Zenith® Fenestrated AAA Endovascular Graft between April 4, 2012 and March 31, 2019, with the number in parentheses indicating the specific number reported in the previous year.

Table 13: Summary of Reportable Complaints from Worldwide Commercial Experience with the Zenith® Fenestrated AAA Endovascular Graft Between April 4, 2012 and March 31, 2019

Complaint/Event	Total US (number new in past year)	Total OUS (number new in past year)
Adverse physiological response	6 (1)[a,i,k]	1 (1)
Coating came off	3 (2)[l]	0 (0)
Damaged stent	1 (0)	0 (0)
Device occluded	2 (0)[d]	0 (0)
Difficult to advance	1 (0)[e]	0 (0)
Difficult to release	6 (1)[h]	0 (0)
Difficult to remove	3 (1)	2 (0)
Difficult to visualize	1 (0)	1 (0)
Disconnection (graft disconnect without separation)	0 (0)	2 (0)[m]
Type I endoleak	6 (2)	1 (0)
Type II endoleak	1 (0)	0 (0)
Type III endoleak*	8 (1)	1 (0)
Foreign matter	1 (0)	0 (0)
Improper graft placement	2 (0)	1 (0)
Inadequate documentation	2 (0)	0 (0)
Incorrect alignment	11 (1)[b]	0 (0)
Incorrect product	2 (1)	0 (0)
Kinked	1 (1)	0 (0)
Knotted suture	1 (0)	0 (0)
Leakage	25 (0)	3 (0)
Migration	2 (0)	0 (0)
Premature deployment	1 (0)	0 (0)
Rupture	1 (0)[c]	0 (0)
Separated (graft separation)*	22 (6)[j]	0 (0)
Strut formation	1 (0)	0 (0)
Vessel occluded	14 (5)[f,g]	4 (4)[n]
Wire not advancing	1 (0)	0 (0)
Not a reject - No defect	6 (2)	1 (1)
To be determined	1 (1)	0 (0)
Total	**132 (25)**	**17 (6)**

Note: Counts reflect the number of complaints received and not necessarily the number of unique patients with a particular event, as multiple complaints for the same event/occurrence may have been received for a given patient (e.g., one event/occurrence triggering multiple complaints equal to the number of graft components placed/involved).

*12 complaints initially recorded as type III endoleaks in the US and reported as such in previous updates have been reclassified as graft separation following further investigation indicating the ZFEN-P and ZFEN-D components separated, causing a type III endoleak.

[a] ZFEN-P. One (1) patient death recorded. Patient expired after placement of device.
[b] ZFEN-P. One (1) patient death recorded. The device twisted and required open surgery. Patient expired 3 days post-surgery.
[c] ZFEN-P. One (1) patient death recorded. Ballooning with CODA caused infrarenal aortic rupture, leading to patient death.
[d] ZFEN-D. One (1) patient death recorded. Perforation in component noticed during and after procedure, and a thrombectomy was performed. Patient expired 2 weeks post procedure.
[e] ZFEN-P. One (1) patient death recorded. Ruptured iliac artery, requiring removal of ZFEN-P. Patient expired during open repair.
[f] ZFEN-P. One (1) patient death recorded. Patient expired due to bowel ischemia.
[g] ZFEN-P. One (1) patient death recorded. 6 months post procedure the SMA and left renal artery were occluded.
[h] ZFEN-P. One (1) patient death recorded. The trigger wire would not release, causing patient death.
[i] ZFEN-P. One (1) patient death recorded. A pseudoaneurysm left of the renal artery ruptured, causing patient death.

[j] ZFEN-P and ZFEN-D. One (1) patient death recorded. Graft separation, causing patient death.
[k] ZFEN-P and ZFEN-D. Three (3) patient deaths recorded. In patient #1, an abdominal aortic aneurysm (AAA) ruptured. Patient #2 died due to bleeding post-procedure. Patient #3 passed away post procedure.
[l] ZFEN-P and ZFEN-D. One (1) patient death recorded. Patient expired 3 days post procedure.
[m] ZFEN-P and ZFEN-D. One (1) patient death recorded. Patient passed away due to graft disconnection, triggering a endoleak.
[n] ZFEN-P. One (1) patient death recorded. Patient expired 2 days post procedure following AAA repair complications.

As indicated by the footnotes in Table 13, there have been 15 deaths reported in conjunction with various complaint types (3 new reports in the previous year). Table 14 further summarizes the reported cause of death in each case. The causes of death were often associated with pre-existing comorbidities and complex patient anatomies, which included tortuous aortas. Importantly, investigation of each death found no evidence to suggest non-conformance or deficiency with the design or manufacturing of the device.

Table 14: Causes of death

Cause of death	**Total US (number new in past year)**	**Total OUS (number new in past year)**
Bowel ischemia	3 (1)	0 (0)
Conversion to open repair	1 (0)	0 (0)
Disconnection (graft disconnect without separation)	0 (0)	1 (0)
Type I endoleak	1 (1)	0 (0)
Graft separation	1 (0)	0 (0)
Infrarenal aortic rupture	1 (0)	0 (0)
Occlusion of Superior Mesenteric Artery (SMA)	0 (0)	1 (1)
Perforated vessel	2 (0)	0 (0)
Post procedure renal failure	1 (0)	0 (0)
Ruptured aneurysm	2 (0)	0 (0)
Stroke/embolization	1 (0)	0 (0)
Total	**13 (2)**	**2 (1)**

Overall, the most frequently reported complaint type has been for (valve) leakage (28 total complaints), with the greatest number occurring in 2014 (24), following which further inspections of the valve were implemented during manufacturing; only 1 complaint has since been reported.

The second-most frequently reported complaint type has been for component separation (22 total complaints), occurring in 13 patients, including 3 new patients (6 complaints) during the past year, prompting the need for further investigation into the known risk . All patients with component separation were treated in the US, whereas there have been no similar reports for patients treated outside the US. As noted earlier, there are design differences between the version of the device available in the US compared to the version

available outside the US; one of the design differences is relevant with respect to the potential for component separation and likely explains the difference in reports between the US and outside the US. Specifically, the version of the device available in the US has the same diameter proximal and distal components overlapping with one another in order to ensure displacement forces preferentially act on the overlap zone (the length of which can be monitored and further extended with use of an ancillary component if the length is reduced over time) rather than the region of the graft containing fenestrations; the version available outside the US has an overlap with an interference fit (larger diameter distal component placed inside a smaller diameter proximal component). Analysis of the complaints was often limited given there was little or no information available regarding the length of overlap upon completion of the procedure and during follow-up. Results from analysis of available information suggested a reduction in overlap length as the aorta elongated and/or graft aligned with the greater curve of the aneurysm over time, and there were no reinterventions performed to extend the overlap once the length was reduced to less than the minimum recommended amount of at least two stents. The investigation found no evidence to suggest non-conformance or deficiency with the design or manufacturing of the device.

Vessel occlusion is the third-most frequently reported complaint overall (18 total) and is also the most frequently reported complaint in the past year (9). Vessels that were reported as having occlusion included: the superior mesenteric artery (SMA), right and left renal arteries, left external iliac artery, and celiac artery. Investigation of reported occlusion related complaints concluded that all complaints were associated with known risks (e.g., inability to control and orientate graft during deployment, partially deployed grafts that cannot be reorientated to align fenestrations with arteries, and graft rotation within the artery post-implantation) with no new risks identified. Notably, investigation of reported occlusion related complaints found no evidence to suggest non-conformance or deficiency with the design or manufacturing of the device.

The frequencies of other reported complaint types remain relatively low.

Section III – Explant Analysis

This section summarizes the findings from explant analysis of grafts from clinical study and worldwide commercial experience. Explant analysis is performed using high resolution X-ray, gross examination, histological microscopy, and scanning electron microscopy. The assessment is focused upon graft material wear, suture wear, and metal component fatigue. While damage from surgical instruments during explantation is sometimes obvious in explant analysis, it is not always possible to determine whether observations occurred before explantation or whether the explantation process contributed to, or caused, the observations.

Clinical Study Experience

There have been no explants analyzed from the multicenter study.

There has been one explant analyzed from noncommercial experiences outside the multicenter study. The implantation time was approximately 170 days. The explant was taken at the time of autopsy from a patient who died following a myocardial infarction. The explant analysis identified barb separations, suture break (green), and cuts in the graft material – there was no evidence of stent fracture or graft material wear.

Worldwide Commercial Experience

There have been no explants analyzed from worldwide commercial experience.

Summary

There has been one explant analyzed. While damage from surgical instruments during explantation was sometimes obvious, it was not always possible to determine whether observations occurred before explantation or whether the explantation process contributed to, or caused, the observations. Nonetheless, routine imaging follow-up remains important to detect any potential compromises in device integrity that might require reintervention.

Section IV – Notes to Clinicians

Component separation has been previously reported with this device, secondary to intercomponent movement resulting from changes in anatomy and/or graft position.[1]

As noted in Section I, there has been one component separation with Type III endoleak and rupture in the post-approval study, which was newly reported since the previous clinical update. The site's report of component separation noted that it occurred in the setting of aortic elongation. Cook's internal review of the follow-up imaging corroborates the site's impression that the reason for separation likely stemmed from aortic elongation, as the length of the aorta from the most inferior renal artery to the aortic bifurcation increased (by 14 mm) from post-procedure to 4 years, while the anterior-posterior distance between L4 and the wall of the graft also increased (by 5.7 mm), the sum of which (19.7 mm) approximated the amount of reduction in component overlap length between components (21.8 mm). Thus, by the 4-year follow-up time point, there was only about a 1-stent overlap length between components, as compared to the minimum recommended overlap length of at least 2 stents, likely owing to the eventual separation that occurred in the subsequent follow-up period.

As noted in Section II, there have been a total of 13 patients with component separation during commercial use. The limited information available similarly suggested a reduction in overlap length as the aorta elongated and/or graft aligned with the greater curve of the aneurysm over time without any reintervention to extend the overlap.

Consistent with the recommendations provided in the IFU (summarized in Section V), it is important to ensure an adequate overlap length not only at the time of procedure, but also during follow-up, with consideration for reintervention in the setting of a decrease in the length of overlap between components, particularly when the length of overlap is less than the 2-stent minimum.

1 Dowdall JF, Greenberg RK, West K, et al. Separation of components in fenestrated and branched endovascular grafting – Branch protection or a potentially new mode of failure? Eur J Vasc Endovasc Surg 2008;36:2-9.

Section V – Brief Summary of Indications, Warnings, and Precautions from IFU

Indications

The Zenith® Fenestrated AAA Endovascular Graft is indicated for the endovascular treatment of patients with abdominal aortic or aortoiliac aneurysms having morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with required introduction systems
- Nonaneurysmal infrarenal aortic segment (neck) proximal to the aneurysms with:
  - Length ≥ 4 mm and unsuitable for a non-fenestrated graft
  - Diameter ≤ 31 mm and ≥ 19 mm
  - Angle < 45 degrees relative to long axis of aneurysm
  - Angle < 45 degrees relative to axis of suprarenal aorta
- Ipsilateral iliac artery fixation site > 30 mm in length and between 9 – 21 mm in diameter
- Contralateral iliac artery distal fixation site > 30 mm in length and between 7 – 21 mm in diameter

Warnings and Precautions

General Use Information

- Intervention or conversion to standard open surgical repair following initial endovascular repair should be considered for patients experiencing enlarging aneurysms, unacceptable decrease in fixation length (vessel and component overlap) and/or endoleak. An increase in aneurysm size and/or persistent endoleak may lead to aneurysm rupture.

Patient Selection

- Key anatomic elements that may affect successful exclusion of the aneurysm include severe proximal neck angulation (> 45 degrees for infrarenal neck to axis of AAA or > 45 degrees for suprarenal neck relative to the immediate infrarenal neck); short proximal aortic neck (< 4 mm); greater than 10% increase in diameter over 15 mm of proximal aortic neck length; and circumferential thrombus and/or calcification at the arterial implantation sites, specifically the proximal aortic neck and distal iliac artery interface. Irregular calcification and/or plaque may compromise the fixation and sealing of the implantation sites. Necks exhibiting these key anatomic elements may be

more conducive to graft migration.

- Patients with recurrent aortic aneurysmal disease or with disease above the renal arteries may be prone to further aortic dilation in the renal/visceral segment, which could compromise device integrity/fixation.

Implant Procedure

- Inaccurate placement and/or incomplete sealing of the Zenith® Fenestrated AAA Endovascular Graft within the vessel may result in increased risk of endoleak, migration, or inadvertent occlusion of the renal or internal iliac arteries. Renal artery patency must be maintained to prevent/reduce the risk of renal failure and subsequent complications. It is recommended that all vessels accommodated by a small fenestration be stented in order to secure positive alignment of the graft fenestration with the vessel origin.

Clinical Use Information

Device Length Sizing Guidelines

The proximal body graft and distal body graft are available in multiple lengths. The chosen lengths should provide a minimum two-stent overlap should the graft components align completely along the greater curve of the aorta/aneurysm over time. Planning for a longer overlap length initially (e.g., 3-4 stents) is therefore preferable.

Imaging Guidelines and Post-operative Follow-up

General

The imaging recommended at follow-up (CT/X-ray) is the same as for a non-fenestrated device and is intended to similarly provide for an assessment of device integrity, endoleak, change in aneurysm size, and device position (migration, component overlap).

Note: Refer to the IFU for complete warnings and precautions