

Conversion

As shown in Table 10, there have been no conversions to open surgical repair in the endovascular treatment group.

Table 10: Kaplan-Meier for Freedom from Conversion

Arm	Days	Kaplan-Meier Estimate	Standard Error	Cumulative Events	Cumulative Censored	Patients remaining
Endovascular	0	1.000	0.0000	0	0	160
	30	1.000	0.0000	0	4	156
	365	1.000	0.0000	0	24	136
	730	1.000	0.0000	0	43	117
	1095	1.000	0.0000	0	62	98
	1460	1.000	0.0000	0	98	62
	1825	1.000	0.0000	0	142	18

Summary

Patient follow-up in the multi-center pivotal clinical study remains on-going and will continue through 5 years. As of March 12, 2010, survival from aneurysm-related mortality at 1095 days was 91.8% in the endovascular treatment group and 88.3% in the open surgical control group. To date, no death in the endovascular treatment group was found to be related to failure of a component of the device. The percent of patients with new endoleak at 36 months was 1.2%, and the percent of patients with an increase in aneurysm/ulcer size was 4.9%, as compared with 59.3% who showed a decrease in size. New device integrity observations at 36 months included 3 patients with barb separation and 1 patient with stent fracture, none of which were clinically significant in terms of requiring reintervention. There has been one report of component separation at 36 months, in the setting of aortic elongation, resulting in Type III endoleak requiring reintervention. No new clinically significant migrations have been reported at 36 months. The percent of patients requiring at least one reintervention subsequent to the initial aneurysm/ulcer repair procedure is 6.9% in the endovascular treatment group and 8.6% for the open surgical control group. There have been no ruptures or conversions to open surgical repair in the endovascular treatment group. These data continue to support the safety and effectiveness of the Zenith® TX2® TAA Endovascular Graft.

Section II – Worldwide Commercial Experience

The Zenith® TX2® TAA Endovascular Graft was commercially available in the US soon after marketing clearance was granted by FDA on May 21, 2008, and has been in commercial use throughout the rest of world (except Japan) since 2004 (Canada in 2009). While the device is indicated in the US to treat only patients with aneurysms or ulcers of the descending thoracic aorta, the approved indications outside the US (except Canada) include treatment of patients with atherosclerotic or enlarging aneurysms, symptomatic acute or chronic dissections, or contained ruptures.

As shown in Table 11, a total of 16,186 components (including 7,842 components in the US) have been distributed worldwide between May 21, 2008 and March 31, 2010.

Table 11: Total Number of Zenith® TX2® TAA Endovascular Graft Components Sold Worldwide (May 21, 2008 through March 31, 2010)

Component	Global Number Sold	US Number Sold
ZTEG-2P (proximal component)	7,943	3,751
ZTEG-2PT (proximal tapered component)	3,029	1,546
ZTEG-2D (distal component)	3370	1,619
ESBE-T (distal body extension)	444	243
TBE (proximal body extension)	1,400	683
Total	16,186	7,842

Cook evaluates product performance from this commercial experience based on complaint reporting systems throughout the world. Table 12 summarizes the procedural and follow-up complaints received during commercial experience with the Zenith® TX2® TAA Endovascular Graft between May 21, 2008 and March 31, 2010. All complaints received related to the Zenith® TX2® TAA Endovascular Graft are processed through the Customer Relations Department of the William Cook Europe Quality System.

Complaints relating to user error, procedural complication, or device malfunction undergo a clinical review by Cook medical personnel. Based on this review, additional information may be requested from the user facility at which the event occurred. Cook medical staff along with the Quality Engineering group make a final determination of root cause, and the findings are evaluated for any necessary corrective action.

Table 12: Complaints from Commercial Experience with the Zenith® TX2® TAA Endovascular Graft between May 21, 2008 and March 31, 2010

Complaint	n
Death	
Early (\leq 30 days)	6 ^{a,b,c,d,e,f}
Late ($>$ 30 days)	0
Serious injury	
Not device related	1 ^g
Proximal dissection	1 ^h
Endoleak	
Type unknown or not reported	1 ⁱ
Required additional intervention	
During procedure	1 ^j
Other	
Difficult to remove trigger wire	2
Difficult trackability due to difficult anatomy	1
Sheath buckling	2
Valve too tight	1
Proximal stent portion failed to open	1 ^k
Total	17

^aDeath due to DIC.

^bDeath due to MI.

^cCause of death unknown.

^dDeath due to complications of procedure; spinal cord infarction and respiratory failure.

^eDeath due to presenting trauma at time of procedure.

^fDeath due to pre-existing condition.

^gHemothorax.

^hProximal extension of dissection in patient with pre-existing dissection.

ⁱResolved following extension placement within 30 days of initial procedure.

^jRepositioning of graft with ballooning for treatment of distal Type I endoleak.

^kLimited information suggests a pre-existing iliac stent may have been carried up with the device and constricted its complete expansion; no flow restriction was reported.

None of the complaints received resulted in corrective or preventative action. The nature and frequency of complaints during this time period are consistent with those observed during periods of commercial use prior to approval in the US.

Section III – Explant Analysis

This section summarizes the findings from explant analysis of grafts from clinical study and worldwide commercial experience.

Clinical Study Experience

In addition to radiographic and clinical data, information was obtained from one explanted device that was submitted as a part of the multi-center clinical study. The device was explanted at the time of autopsy following death unrelated to aneurysm repair or a failure in device integrity.

While damage from surgical instruments during explantation is sometimes obvious in explant analysis, it is not always possible to determine if observations occurred before explantation or if the explantation process contributed to, or caused, the observations. Explant analysis was performed using high resolution X-ray, gross examination, histological microscopy, and scanning electron microscopy. The assessment was focused upon graft material wear, suture wear, and metal component fatigue.

The length of implant in the one explant was 222 days. The observations from explant analysis are listed in Table 13.

Table 13: Observations from Grafts Explanted during the Multi-center Clinical Study

Reason for explant	Days Implanted	Observations ¹					
		Damaged or Broken Stents	Barb Separation	Graft Wear	Cut or Broken Sutures (green) ²	Cut or Broken Sutures (blue) ³	Suture Hole Elongation
Autopsy (unrelated death)	222			1 ⁴	3		1

¹ Noted observations may have been due to damage caused during explantation.

² Sutures used to attach external stents.

³ Sutures used to attach internal stents and bare stent.

⁴ Not associated with endoleak.

Three explants from other non-commercial experiences outside the multi-center study have been analyzed. None of the explantation procedures were due to failure in device integrity, and the mean implantation time was 394 days (range of 20 to 711 days). None of the explants were found to have graft wear or damaged/broken stents. Two explants had barb separation; however the barb wire was smaller in diameter than what is

currently available. Each explant had cut or broken sutures (green). One explant had cut or broken sutures (blue), and one explant had suture hole elongation. While damage from surgical instruments during explantation was sometimes obvious, it was not always possible to determine if observations occurred before explantation or if the explantation process contributed to, or caused, the observations.

Worldwide Commercial Experience

There have been no explants analyzed from worldwide commercial experience.

Summary

In total, there have been four explants analyzed. None of the explants analyzed were explanted due to failure in device integrity, and there were no reported adverse clinical sequelae associated with the post-explant observations, which may have been due to damage caused during explantation. Nonetheless, routine imaging follow-up remains important in detecting any potential compromises in device integrity that might require reintervention.

Section IV – Notes to Clinicians

At this time, there are no additional notes or instructions to clinicians beyond what is already described in the IFU – the key aspects are briefly summarized in Section V.

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

Indications

The Zenith® TX2® TAA Endovascular Graft is indicated for the endovascular treatment of patients with aneurysms or ulcers of the descending thoracic aorta having morphology suitable for endovascular repair, including:

- Adequate iliac/femoral access compatible with the required introduction systems,
- Non-aneurysmal aortic segments (fixation sites) proximal and distal to the aneurysm or ulcer:
 - With a length of at least 25 mm, and
 - With a diameter measured outer wall to outer wall of no greater than 38 mm and no less than 24 mm.

Warnings and Precautions

Patient Selection

- The Zenith® TX2® TAA Endovascular Graft is designed to treat aortic neck diameters no smaller than 24 mm and no larger than 38 mm. The Zenith® TX2® TAA Endovascular Graft is designed to treat proximal aortic necks (distal to either the left subclavian or left common carotid artery) of at least 25 mm in length. Additional proximal aortic neck length may be gained by covering the left subclavian artery (with or without discretionary transposition) when necessary to optimize device fixation and maximize aortic neck length. A distal aortic neck length of at least 25 mm proximal to the celiac axis is required. These sizing measurements are critical to the performance of the endovascular repair.
- Key anatomic elements that may affect successful exclusion of the aneurysm or ulcer include a radius of curvature <35 mm; localized aortic neck angulation >45 degrees; short proximal or distal fixation sites (<25 mm); an inverted funnel shape at the proximal fixation site or a funnel shape at the distal fixation site (greater than 10% change in diameter over 25 mm of fixation site length); and circumferential thrombus and/or calcification at the arterial fixation sites. In the presence of anatomical limitations, a longer neck length may be required to obtain adequate sealing and fixation. Irregular calcification and/or plaque may compromise the attachment and

sealing at the fixation sites. Neck exhibiting these key anatomic elements may be more conducive to graft migration or endoleak.

Device Selection

- The recommended amount of overlap between devices is 3-4 stents. However, the proximal sealing stent of the proximal component or distal sealing stent of the distal component should not be overlapped, as doing so may cause malapposition to the vessel wall. The minimum required amount of overlap between devices is 2 stents (~50 mm) – less than 2 stents may result in endoleak (with or without component separation). Device lengths should be selected accordingly.
- Strict adherence to the Zenith® TX2® TAA Endovascular Graft IFU sizing guide is strongly recommended when selecting the appropriate device size. Appropriate device oversizing has been incorporated in the IFU sizing guide. Sizing outside of this range can result in endoleak, fracture, migration, device infolding, or compression.

Implant Procedure

- Do not bend or kink the delivery system. Doing so may cause damage to the delivery system and the Zenith® TX2® TAA Endovascular Graft.
- Do not continue advancing the wire guide or any portion of the delivery system if resistance is felt. Stop and assess the cause of resistance; vessel, catheter, or graft damage may occur. Exercise particular care in areas of stenosis, intravascular thrombosis, or calcified or tortuous vessels.
- Repositioning the stent graft distally after partial deployment of the covered proximal stent may result in damage to the stent graft and/or vessel injury.
- Landing the proximal and distal ends of the device in parallel aortic neck segments without acute angulation (>45 degrees) or circumferential thrombus/calcification is important to ensuring fixation and seal.
- Landing the proximal or distal ends of the device in an aortic neck segment with a diameter that differs from that to which the graft was sized initially may potentially result in inadequate sizing (<10% or >25%) and therefore migration, endoleak, aneurysm or ulcer enlargement, or increased risk of thrombosis.

Note: Refer to the IFU for complete warnings and precautions