From the Society for Vascular Surgery

Pivotal results for the Valiant Navion stent graft system in the Valiant EVO global clinical trial

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ABSTRACT

Objective: The Valiant Navion stent graft system (Medtronic, Santa Rosa, Calif) is a new iteration of a thoracic endograft for the treatment of descending thoracic aortic aneurysms. Herein, the 30-day primary safety and efficacy outcomes and secondary end points are presented.

Methods: The Valiant EVO global clinical trial is a prospective, nonrandomized, single-arm trial. Patient enrollment occurred from April 2016 to October 2017. The primary end point was defined as access and/or deployment failure and/or a major device effect (MDE), including device-related secondary procedures, device-related mortality, conversion to open surgery, or thoracic aortic aneurysm rupture within 30 days of the index procedure. Other measures of stent graft performance including procedural data, rates of secondary procedures, and frequency of endoleaks are also reported.

Results: Of the 87 consecutive patients undergoing thoracic endovascular aneurysm repair who were enrolled, 33 (37.9%) were female with 61 (70.9%) presenting with severe access artery tortuosity and 66 (85.7%) with high thoracic aortic tortuosity per core laboratory evaluation. The mean procedure duration was 88.7 ± 53.4 minutes and geographical differences existed such as percutaneous access (37/52 [71.2%]) in the United States and surgical cut down in the outside of the U.S. sites (28/35 [80.0%]). There were no access or deployment failures and only 2.3% of the patients (2/87; $P < .0001$; performance goal of 16%) experienced a MDE within 30 days of the index procedure. Two secondary procedures (n = 1 retrograde type A dissection; n = 1 aortic arch rupture) were required, and in the first 30 days, two patients died leading to a freedom from all-cause mortality of 97.7%. Endoleaks at 1 month were reported in 2.5% of patients (n = 1 type Ia; n = 1 type II).

Conclusions: Access/deployment failures, MDEs, and endoleaks were rare in the first 30 days of the Valiant Evo clinical trial. The Valiant Navion thoracic stent graft system has shown encouraging 30-day results in this challenging cohort and trial patients will continue to be followed through 5 years. (J Vasc Surg 2019;■:1-10.)

Keywords: Thoracic endovascular aortic repair; Thoracic stent graft; TEVAR

Thoracic endovascular aneurysm repair (TEVAR) is a minimally invasive method of repairing thoracic aortic aneurysms (TAAs) and is associated with reduced mortality, perioperative morbidity, and shorter hospital stays compared with open surgical repair.[1,2] Although the long-term outcomes and durability are often a concern for endovascular repair strategies, TEVAR has been reported to have low reintervention and aneurysm related mortalities through 5 years.[3-5] In addition, TEVAR outcomes are continuously improving over time as a result of increased operator experience and evolution of stent graft designs and accompanying equipment.[6] As a result, TEVAR is widely accepted as the standard of care for TAAs.

A current limitation for the TEVAR procedure can be the patient's anatomic characteristics. The standard TEVAR procedure consists of a femoral introduction of the device. In patients with highly tortuous access

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vessels, and also in women who have smaller diameter access arteries, the introduction of a larger profile delivery system can lead to an increased risk for access related complications.[7,8] Similar to endovascular abdominal aortic repair, a challenging TEVAR landing zone, which could consist of a short proximal neck, curvature, or severe angulation, is also associated with an increased risk of adverse events and endoleaks.[9-11] The latest versions of thoracic stent grafts seek to overcome the limitations of previous generation devices by using smaller profile delivery systems and having improved stent graft apposition to the aortic wall for varied patient anatomies.

The Valiant Navion stent graft system (Medtronic Inc, Santa Rosa, Calif) is a third-generation TEVAR device designed to allow for better delivery and conformability. Compared with the prior generation stent graft, the Valiant Captivia system,[2,3] the Navion device has a reduced delivery system profile and is available in an outer diameter of 18F, 20F, or 22F and a working length of 93 cm (Fig 1). The catheter assembly is entirely compatible with a 0.035-in (0.89-mm) guidewire and has a tip-capture two-step deployment system. The catheter assembly has a flexible and hydrophilic-coated taper tip to facilitate vessel access, which is approximately 1 cm shorter than the earlier generation system. Radiopaque markers on the stent graft as well as the nitinol stents are both visible under fluoroscopy and allow for accurate positioning and deployment of the stent graft.

Navion stent grafts are offered in 60, 100, 175, and 225 mm straight or tapered lengths and a single graft may be used if it provides sufficient coverage, or additional grafts can be used in combination to increase the length. The proximal end is offered with a bare stent (FreeFlo) or without a bare stent (CoveredSeal) configuration to accommodate patient specific anatomies and scenarios (Fig 1). All configurations can be used either as a proximal or distal component. The FreeFlo configuration is indicated for a nonaneurysmal aortic proximal neck length of 20 mm or greater and the CoveredSeal configuration requires a 25 mm or greater proximal neck length. Herein, the 30-day primary safety and effectiveness results along with procedural and clinical outcomes with the Navion stent graft in the Valiant Evo clinical trial are reported.

ARTICLE HIGHLIGHTS

- **Type of Research:** Prospective, nonrandomized, single-arm trial conducted under a US Food and Drug Administration Investigational Device Exemption
- **Key Findings:** Eighty-seven patients with descending thoracic aortic aneurysms were treated with the Valiant Navion stent graft. The primary end point was achieved with no access or deployment failures; 2.3% of patients experienced a major device effect through 30 days of follow-up. Two patients underwent secondary procedures and the freedom from all-cause mortality was 97.7% through 30 days.
- **Take Home Message:** In the Valiant Evo clinical trial, the 30-day results were encouraging with no access or deployment failures and a low incidence of major device effects, endoleaks, and secondary procedures.

METHODS

Trial enrollment. The Valiant Evo US and International Clinical Trials (NCT02625324 and NCT02652949) were prospective, nonrandomized, single-arm trials designed to evaluate the safety and effectiveness of the Valiant Navion thoracic stent graft system in patients with a descending TAA (DTAA) and penetrating atherosclerotic ulcers (PAUs). The Valiant Evo U.S. Clinical Trial was conducted under an U.S. Food and Drug Administration Investigational Device Exemption and the Valiant Evo International Clinical Trial was conducted in compliance with the international standards and relevant reporting laws. All patients in the trials provided written informed consent and the institutional review board of the participating institutions approved the clinical investigation plan before patient enrollment. Both trials were conducted in compliance the Declaration of Helsinki (October 2013) and the laws and regulations of the countries in which the clinical trials were conducted.

The inclusion and exclusion criteria for the Valiant Evo trials are listed in the Appendix (online only) and are comparable with previous thoracic stent graft trials.[2] One difference is the Valiant Evo trials allowed for the inclusion of patients with smaller proximal and distal neck diameters (16 mm instead of the previous 20 mm) owing to the availability of smaller diameter stent grafts (20 mm instead of the previous 22 mm). A total of 139 patients were consented and reviewed for eligibility by the independent physician reviewer, of whom 52 patients were screen failures most commonly owing to not meeting all imaging assessed anatomy criteria or having already received a previous aortic graft or repair. Thus, 87 patients were enrolled between April 2016 and October 2017, with 18 participating U.S. sites enrolling 59.8% of the cohort (52/87) and 13 sites outside of the United States (OUS) enrolled the other 40.2% of patients (35/87).

End points and definitions. The primary end point was an assessment of the proportion of patients who experienced a composite safety and effectiveness event. The composite measure included access and/or deployment failures, and/or a major device effect (MDE) within 30 days of the index procedure. Per the study protocol, access failure is defined as the inability to insert a device owing to mechanical failure or anatomic exclusions of the femoral or iliac arteries. The definition of a MDE included device-related secondary procedures, device-related mortality, conversion to open surgery, or TAA rupture.

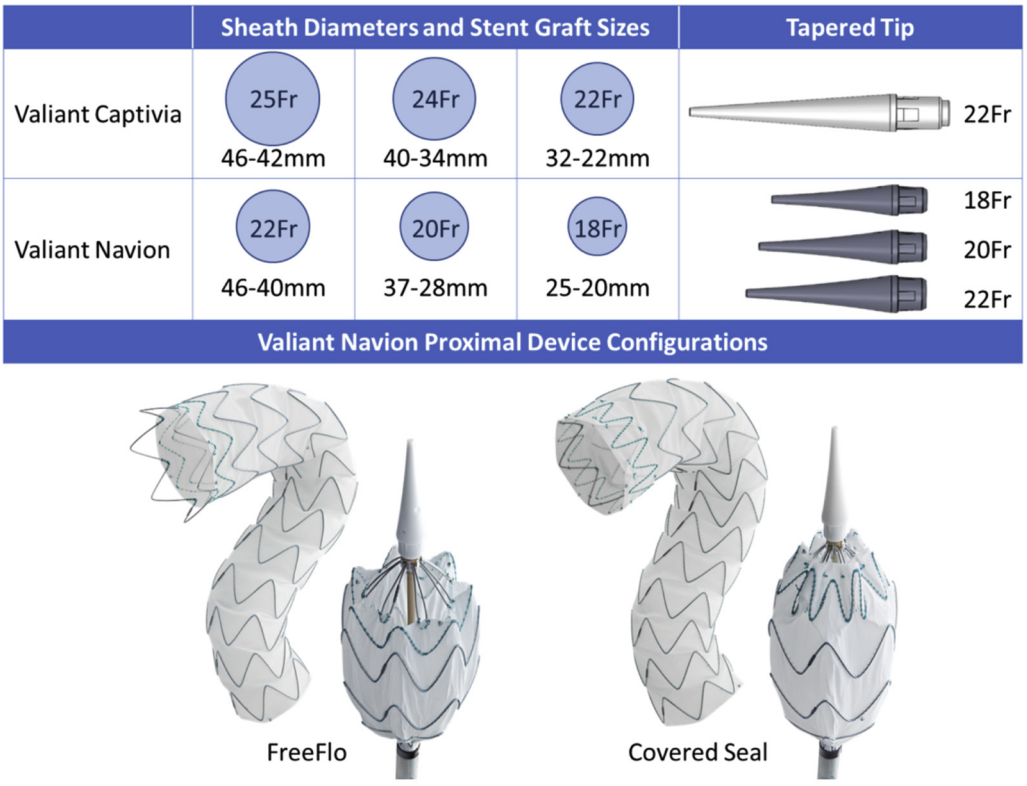


Fig 1. Valiant Navion delivery system and graft configurations.

All patients were originally consented to follow-up evaluations at 30 days, 6 months, and 1 year, although the study was later extended with a portion of patients having yearly follow-up to 5 years. Secondary end points of the trial include measurements of perioperative mortality within 30 days; all-cause mortality (ACM) and aneurysm-related mortality (ARM) are to be evaluated at all follow-ups from 6 months through 5 years. MDEs, all adverse events, secondary procedures, and endoleaks are to be monitored at all follow-ups from 6 months through 5 years. Core laboratory-assessed stent graft patency is reported at 30 days. Other performance measures such as migration were defined based on comparisons with the 30-day imaging, thus requiring longer follow-up, and are not reported herein. Artery tortuosity was defined as the centerline length divided by the straight line length from proximal to distal end of the artery with values of less than 1.1 considered mild, 1.11 to 1.18 moderate, and 1.19 or greater severe. The definitions of the secondary end points are similar to those described in detail in earlier thoracic stent graft trials.[2]

Statistical analysis. The primary end point of the study was tested against a performance goal of 16%. This was a literature-derived estimate[12] considered sufficient for regulatory use as a safety and effectiveness end point and comparable with the U.S. Food and Drug Administration-approved performance goals of other TEVAR studies (NCT00435942, NCT00874250). The primary end point was considered successfully achieved if the null hypothesis was rejected with a one-sided binomial test at a statistical level of 0.025. The sample size of 87 patients, performance goal, and significance level was determined to provide at least 80% statistical power for the primary hypothesis.

Baseline patient and anatomic characteristics along with the secondary outcomes were summarized descriptively. Continuous variables are presented with a mean ± standard deviation or with a median (minimum, maximum) and categorical variables are reported as percentage of patients. Time to MDEs, ACM, and ARM are analyzed with Kaplan-Meier survival analyses with the Greenwood method used for the standard error estimate. All statistical analysis was performed using SAS (version 9.1 or higher, SAS Institute Inc, Cary, NC).

RESULTS

Baseline patients and anatomic characteristics. Patients had a mean age of 70.8 ± 8.7 years and 37.9% (33/87) were female. Race data were not collected in the OUS per regulations, but 78.8% (41/52) of the U.S. patients were white. The medical history of the patients, American Society of Anesthesiologists physical status classification, and primary indication for TEVAR are listed in Table I. Of note, the most common diagnoses at baseline included hypertension and hyperlipidemia. Of

Table I. Patient medical history and American Society of Anesthesiologists (*ASA*) classification

Patient medical history	U.S. and OUS (N = 87)
Cardiovascular	
Carotid artery disease	20.2 (17/84)
Angina	10.3 (9/87)
Arrhythmia	27.6 (24/87)
Congestive heart failure	12.6 (11/87)
Coronary artery disease	35.6 (31/87)
Myocardial infarction	16.1 (14/87)
Abdominal aortic aneurysm	25.3 (22/87)
Ascending thoracic aneurysm	11.5 (10/87)
Peripheral vascular disease	16.3 (14/86)
Hypertension	89.7 (78/87)
Cerebrovascular/neurologic	
Stroke/cerebral vascular accident	9.2 (8/87)
Transient ischemic attack	8.0 (7/87)
Paraparesis	0.0 (0/87)
Paraplegia	0.0 (0/87)
Diabetes	20.7 (18/87)
Hyperlipidemia	73.3 (63/86)
Tobacco use in the last 10 years	51.2 (44/86)
Chronic obstructive pulmonary disease	32.6 (28/86)
Renal insufficiency	21.8 (19/87)
ASA physical status classification	
I	6.9 (6/87)
II	21.8 (19/87)
III	44.8 (39/87)
IV	26.4 (23/87)
Primary indication for TEVAR	
Fusiform aneurysm	42.5 (37/87)
Saccular aneurysm	36.8 (32/87)
PAU	20.7 (18/87)

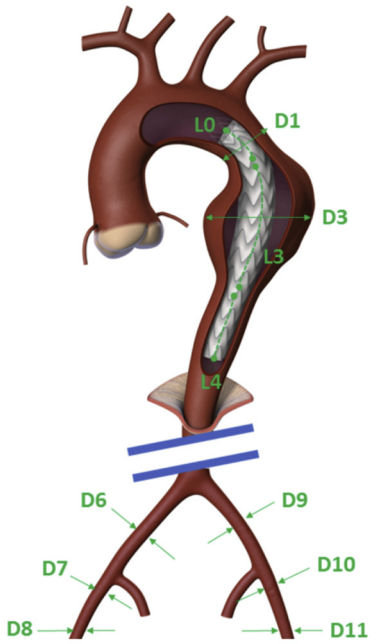
OUS, Outside of the United States; *PAU*, penetrating atherosclerotic ulcer; *TEVAR*, thoracic endovascular aneurysm repair; *U.S.*, U.S., cohort. Data are presented as percent (n/N).

the 87 patients, 62 (71.3%) were classified as American Society of Anesthesiologists class III or IV with 37 of the 87 patients (42.5%) having a fusiform aneurysm, 32 (36.8%) with saccular aneurysms, and 18 (20.7%) with PAUs.

Full baseline measurements of vessel diameters and accessibility were assessed by the core laboratory and are reported in Fig 2. The mean proximal neck diameter and length was 29.3 ± 3.6 mm and 58.9 ± 44.1 mm, respectively. The mean maximum aneurysm diameter and length was 55.7 ± 13.1 mm and 113.1 ± 71.5 mm, respectively. The landing zones for the stent grafts were mildly tortuous (65/87 [74.7%]) with mostly insignificant or no presence of thrombus and calcification (Fig 3). In total, 74.7% of the patients (65/87) received a FreeFlo device as the proximal configuration, and 25.3% (22/87) had a CoveredSeal devices as the proximal stent. The FreeFlo configuration was more often landed in zone 2 (20/65 [30.8%]) and zone 3 (31/65 [47.7%]), whereas the CoveredSeal was used more distally in zone 3 (9/22 [40.9%]) and zone 4 (11/22 [50.0%]). The tapered grafts were less commonly used as the proximal component with only 16 of 65 the patients (24.6%) with a FreeFlo component and 3 of the 22 patients (13.6%) with the CoveredSeal component getting the tapered configuration. The majority of patients (56.3%, 49/87) only received one graft, 36.8% (32/87) had two devices implanted, and 6 of the 87 (6.9%) received three or more grafts. Of the 35 OUS patients, 23 (65.7%) had only one graft implanted compared with 26 of the 52 U.S. patients (50.0%). Receiving three or more devices was more common in the United States (6/52 [11.5%]); no patients in the OUS group required three or more devices. The most common reason for using multiple devices was a long aneurysm that required more than one graft to obtain adequate seal both proximally and distally.

Procedural results. Acute procedural observations at the time of implant are reported in Table II. Differences based on geography were apparent, such as U.S. patients almost exclusively having general anesthesia (51/52 [98.1%]) whereas OUS anesthesia varied with some patients receiving it locally (3/35 [8.6%]) or spinally (2/35 [5.7%]). Percutaneous access was the preferred method in the United States (37/52 [71.2%]), whereas surgical cut down was more common OUS (28/35 [80.0%]). The median radiation exposure higher in the United States (733 mGy; minimum, 31; maximum, 8502) compared with OUS (290 mGy; minimum, 35; maximum, 1654). U.S. patients also spent longer in the intensive care unit (ICU), with a median stay of 64 hours (minimum, 14; maximum, 584) compared with OUS (24 hours; minimum, 17; maximum, 48). The most common preoperative adjunctive procedures was left carotid to left subclavian bypass (11/87 [12.6%]). The most common intraoperative adjunctive procedures were balloon catheterization (27/87 [31.0%]), cerebrospinal fluid (CSF) drainage (15/87 [17.2%]), and left subclavian embolization/occlusion (10/87 [11.5%]). Complete or partial coverage of the left subclavian artery (LSA) occurred in 25.3% of patients (22/87) and only three of these patients (one with complete LSA coverage, two with partial LSA coverage) did not have a revascularization procedure. Revascularization was accomplished with either preoperative or intraoperative left subclavian transposition in seven patients and left carotid to left subclavian bypass in 17 patients.

Primary end point. The primary end point was successfully met with a *P* of less than .0001. Only 2 of the 87 patients (2.3%) experienced the composite safety and effectiveness end point, which was lower than the



Diameter Measurements (mm)	
D1: Proximal Neck	29.3 ± 3.6 (87)
D3: Maximum Aneurysm	55.7 ± 13.1 (87)
D6: Minimum Left CI	9.7 ± 2.5 (86)
D7: Minimum Left EI	7.7 ± 1.9 (85)
D8: Minimum Left Femoral	7.8 ± 1.7 (83)
D9: Minimum Right CI	9.8 ± 2.5 (86)
D10: Minimum Right EI	7.5 ± 1.8 (85)
D11: Minimum Right Femoral	7.7 ± 1.6 (83)
Length Measurements (mm)	
L0: Proximal Neck	58.9 ± 44.1 (87)
L3: Aneurysm (centerline)	113.1 ± 71.5 (87)
L4: Distal Neck	99.0 ± 68.9 (87)

LCCA = left common carotid artery, LSA = left subclavian artery, CI = common iliac, EI = external iliac. *Proximal neck measured as aorta diameter 2 cm proximal to aneurysm

Fig 2. Preimplant vessel and aneurysm measurements from the core laboratory.

performance goal of 16% and was statistically significant with a one-sided 97.5% upper confidence limit of 8.06%. Although the composite end point included access and deployment failures in addition to MDEs within 30 days of the index procedure, no patients were reported to have vessel access or deployment failures.

Of the two patients with MDEs (Table III), one experienced a retrograde type A dissection (RTAD). The patient had site reported aortic diameters of 35 mm at 2 cm proximal to the aneurysm and 36 mm immediately proximal to the aneurysm. The aneurysm was located 28 mm from the left common carotid artery, 19 mm from the LSA, and had a maximum diameter of 50 mm. The patient received a 43-mm proximal graft with the bare stent configuration and balloon angioplasty was used during the implant procedure. The patient experienced pericardial effusion, cardiac tamponade, and hemorrhagic shock in the ICU on day 1 after the procedure. Pericardiocentesis was performed, but severe bleeding at the aortic root in the left coronary ostium could not be controlled and the patient experienced a device-related mortality on day 1. The second patient experienced a complicated recovery and on day 5 had septicemia after infection in a peripheral venous catheter. This complication led to a secondary stent graft infection and contained rupture of the aortic arch on day 28 after the procedure. The patient underwent a device-related secondary procedure to treat a TAA rupture, but subsequently died on day 35 after the procedure.

Secondary end points. The survival rate from ACM and ARM was 97.7% and 97.7% from treatment to 30 days, respectively (Table III). Details of the patient with the RTAD and who died on day 1 are described elsewhere in this article. A second patient underwent a successful implant procedure with no observed postoperative endoleaks or other abnormal findings on their postoperative computed tomography scan. The patient had an uncomplicated recovery but died on day 24 without symptoms before death according to hospital records. The clinical events committee adjudicated this death as an aneurysm-related mortality because it occurred within the first 30 days, but deemed it not device related.

Major adverse events in the first 30 days are presented in Table IV and the overall percentage of patients who experienced one or more major adverse event between 0 and 30 days was 28.7% (25/87). There were a total of five neurologic events, with a stroke rate of 4.6% (4/87, two were posterior and two were hemispheric) and a 1.1% rate (1/87) of spinal cord ischemia. All cerebrovascular accidents were nondisabling and resolved within 1 month. The case of spinal cord ischemia resolved with CSF drainage. A total of two secondary procedures

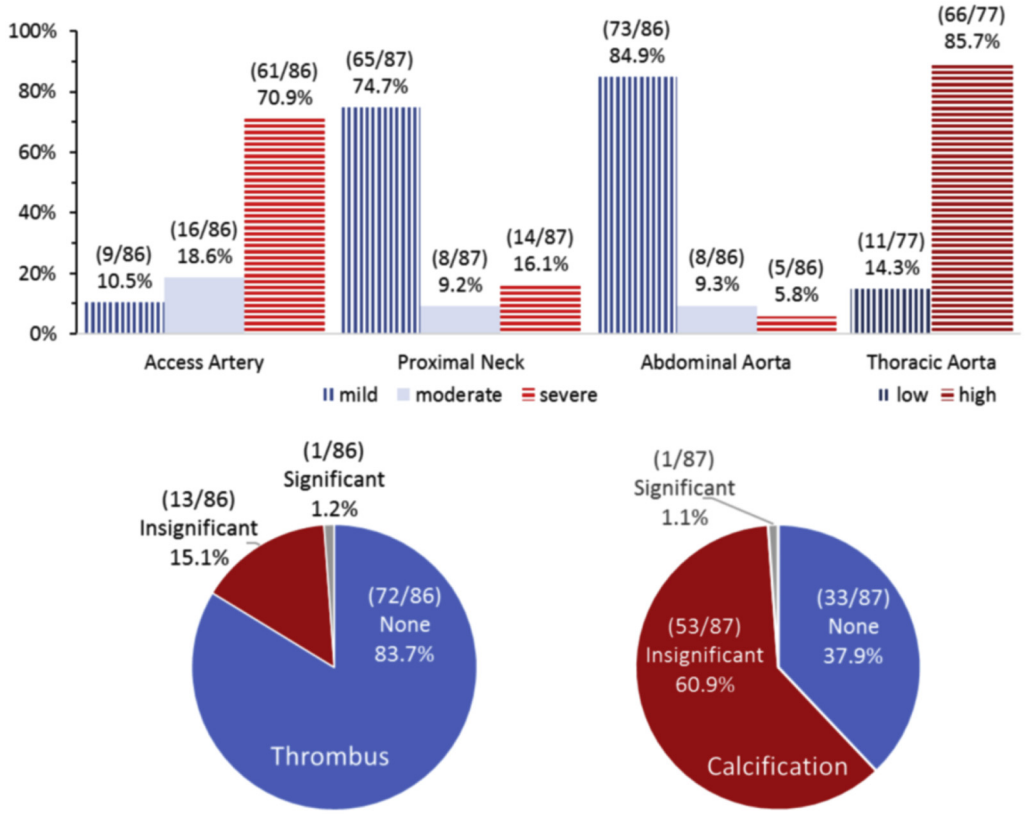


Fig 3. Vessel tortuosity, thrombus, and calcification.

were required within 30 days of the index procedure (days 1 and 28) as detailed elsewhere in this article. The Core laboratory reported one type 1a endoleak and one type II endoleak for an overall endoleak rate of 2.5% (2/81) at the 1-month follow-up, although these two endoleaks were not reported by the respective sites in their end of index procedure imaging. No intervention was undertaken for the two patients with endoleaks. The patient with the type Ia endoleak had subsequent follow-up imaging at 6 months and no aneurysm growth was reported. According to the core laboratory, no loss of patency was reported for any patient at 30 days.

DISCUSSION

In the Valiant Evo clinical trials, patients had positive 30-day results. Despite the challenging anatomies in this cohort, there were no access or deployment failures. Along with the low incidence of type Ia endoleaks and secondary procedures, other outcomes such as mortality and adverse event rates show improvement from earlier TEVAR trials. The Valiant Evo patients will be continued to be followed through 5 years to assess the long-term performance of this thoracic stent graft.

The composite primary end point was achieved with only 2.3% of the patients having a MDE and no access or deployment failures within the 30 days after the index procedure ($P < .0001$; performance goal of 16%). In context with the previously published Bolton Relay Pivotal and Valor II trial results, an ACM of 5.3%[13] and an ARM of 3.1%[2] were reported at 30 days whereas the Valiant Evo trial had a 2.3% ACM and a 2.3% ARM. Because the earlier trials started enrollment in 2006 and 2007, there is a certain degree of improvement expected over time.[14] Increased operator experience and proficiency in endovascular repair is associated with better outcomes[6,15] and this also likely benefitted the patients in the Valiant Evo trials.

RTADs after TEVAR for DTAAs are rare and associated with a high mortality rate should they occur. Previous meta analyses reported a 2.5% incidence rate of RTAD after TEVAR while single study reports vary from 1.3% to 8.0% owing to different patient populations and preconditions.[16-18] In this cohort, one patient (1.1%) had a RTAD as described in detail previously. Some may be concerned with having a proximal graft with the bare stent configuration, although there are conflicting reports as to the effect of a proximal bare stent on RTAD rates.[16,19] A greater degree of oversizing is associated with an increased risk for RTAD, but the Society of Vascular Surgery has not reached a consensus on an optimal oversizing for TEVAR.[20] Other factors such as more angulated landing zones, a history of smoking, and hypertension have also been reported to be associated with increased RTAD rates.[16,17,19] Further insights of the risk factors for

Table II. Procedural observations and clinical usefulness measures

Acute procedural data	U.S. (n = 52)	OUS (n = 35)	U.S. and OUS (N = 87)
Duration of procedure, minutes	87.2 ± 44.2 (52/52)	91.0 ± 65.5 (35/35)	88.7 ± 53.4 (87/87)
Anesthesia type			
General	98.1 (51/52)	85.7 (30/35)	93.1 (81/87)
Local	1.9 (1/52)	8.6 (3/35)	4.6 (4/87)
Epidural	0.0 (0/52)	0.0 (0/35)	0.0 (0/87)
Spinal	0.0 (0/52)	5.7 (2/35)	2.3 (2/87)
Access type			
Surgical cut down	28.8 (15/52)	80.0 (28/35)	49.4 (43/87)
Percutaneous	71.2 (37/52)	20.0 (7/35)	50.6 (44/87)
Estimated blood loss, mL	80.7 ± 144.0 (52/52)	115.0 ± 151.7 (33/35)	94.0 ± 147.1 (85/87)
Patients requiring blood transfusion	3.8 (2/52)	0.0 (0/35)	2.3 (2/87)
Volume of blood transfused, mL	600.0 ± 0.0 (2/52)	NA (0/35)	600.0 ± 0.0 (2/87)
Volume of contrast, mL	96.8 ± 55.6 (52/52)	95.2 ± 49.2 (35/35)	96.2 ± 52.8 (87/87)
Total fluoroscopic time, minutes	13.4 ± 9.3 (52/52)	10.6 ± 8.0 (35/35)	12.2 ± 8.8 (87/87)
Median radiation exposure, mGy	732.5 (48/52) [31, 8502]	290.0 (20/35) [35, 1654]	550.0 (68/87) [31, 8502]
Median time in ICU after index procedure, hours	64.0 (47/52) [14, 584]	24.0 (16/35) [17, 48]	46.0 (63/87) [14, 584]
Time to hospital discharge, days	7.5 ± 6.7 (52/52)	6.6 ± 6.7 (34/35)	7.1 ± 6.7 (86/87)

ICU, Intensive care unit; *OUS*, outside of the United States; *U.S.*, U.S., cohort.
Data are presented as mean ± standard deviation (n/N), percent (n/N), or percent (n/N) [minimum, maximum].

Table III. Kaplan-Meier estimates of freedom from all-cause mortality (*ACM*), aneurysm-related mortality (*ARM*), and major device effects (*MDEs*) through 30 days

	ACM	ARM	MDEs
No. at risk[a]	87	87	87
No. of events	2	2	2
No. censored[b]	7	7	8
Kaplan-Meier estimate[c]	0.977	0.977	0.976
Standard error	0.016	0.016	0.017

[a]Number of patients at risk at the beginning of the study.
[b]Patients censored because their last follow-up occurred before 30 days, while pending their 6-month follow-up.
[c]Estimate made at end of time interval.

RTAD after TEVAR are limited by only having a single RTAD event in this trial.

Access artery complications are becoming a greater concern for endovascular solutions as the potential patient population to be treated with these devices is broadened. Women tend to have smaller and more tortuous access arteries, resulting in more frequent use of the iliac artery, which is associated with an increased risk for adverse events.[7,21] The approximately 40% female study population in the Valiant Evo trial is very consistent with previous clinical trials although the fraction of women is slightly lower in real-world TEVAR registries where men comprise 70% to 80% of the patient population.[12,22,23] In addition to the large proportion of females in the trials, core laboratory imaging graded 70.9% and 85.7% of the Valiant Evo patients as having severe access artery and high thoracic aorta tortuosity, respectively. Access artery tortuosity can result in a more complicated TEVAR if additional intraoperative procedures such as iliac stenting, or endo- or open iliac conduits become necessary.[24,25] Despite the challenging cohort that was treated in this trial, there were no access artery failures. Four patients required the use of iliac stenting, but there was no placement of access artery conduits for tortuosity.

Fewer type Ia endoleaks are associated with improved sac regression and a lesser need for secondary procedures.[26-28] Because patient anatomies and aortic morphologies are unique and varied, contributing to the complexity of landing zones,[29] the two types of proximal stent graft configurations allow operators to customize the therapy to fit the patient's specific needs. The FreeFlo device allows for landing at the distal margin of a supra-aortic vessel while preserving transvessel flow similar to other bare stent designs.[30] The CoveredSeal device, primarily used in more distal aortic zones in this study, offers physicians the option of no exposed bare metal proximal to the stent graft fabric.[31,32] Regardless of proximal device configuration, only one patient in the Valiant Evo trials experienced a type Ia endoleak. Notably, the landing zones for the patients in the Valiant Evo trial were mildly tortuous with mostly insignificant thrombus and calcification.

The rates of other major adverse events were consistent with previous TEVAR devices. In the Valiant Evo trial, the neurologic complication rate was 5.7%, which is

Table IV. Site-reported major adverse events through 30 days

Adverse events[a]	0-30 Days
One or more major adverse events[b]	28.7 (25/87)
Cardiac disorders	17.2 (15/87)
Acute myocardial infarction	1.1 (1/87)
Atrial fibrillation	4.6 (4/87)
Atrial tachycardia	1.1 (1/87)
Atrioventricular block	1.1 (1/87)
Atrioventricular block, first degree	2.3 (2/87)
Cardiac failure, congestive	2.3 (2/87)
Left ventricular failure	1.1 (1/87)
Sinus bradycardia	1.1 (1/87)
Sinus tachycardia	2.3 (2/87)
Supraventricular tachycardia	1.1 (1/87)
Tachycardia	1.1 (1/87)
Ventricular extrasystoles	1.1 (1/87)
Ventricular tachycardia	1.1 (1/87)
Nervous system disorders	5.7 (5/87)
Stroke	4.6 (4/87)
Spinal cord ischemia	1.1 (1/87)
Renal and urinary disorders	3.4 (3/87)
Renal failure, acute	3.4 (3/87)
Respiratory, thoracic, and mediastinal disorders	4.6 (4/87)
Acute respiratory failure	1.1 (1/87)
Atelectasis	2.3 (2/87)
Pulmonary embolism	1.1 (1/87)
Vascular disorders	5.7 (5/87)
Aortic dissection[c]	2.3 (2/87)
Aortic rupture	1.1 (1/87)
Femoral artery occlusion	1.1 (1/87)
Peripheral ischemia[d]	1.1 (1/87)

[a]Patient may report multiple adverse events and in different categories. The total number of patients in each category, including any major adverse event, may not be the sum of those in each subcategory. Each participant was only counted once in each category.
[b]Reported as percent (n/N) of participants who experienced one or more major adverse events.
[c]RTAD case described in results section. The other dissection was focal aortic dissection at the distal end of the graft that was monitored with no treatment planned.
[d]Patient had left hand ischemia.

comparable with previous TEVAR studies with reported rates of between 7.5% and 12.1%.[12,13] In this trial, three strokes were zone 2 coverage, of which two had left subclavian revascularization; the fourth stroke was a zone 4 coverage. For context, a systemic review concluded there was an increased risk for stroke with LSA coverage which is mitigated with revascularization.[33] Vascular complications occurred in 5.7% of Evo trial patients, which is lower than the 22.5%[34] and 20.6%[2] found with other stent grafts, and this could be a reflection of the improved device characteristics. The occurrence of other adverse events such as the cardiovascular complications (17.2% vs 15.6%[34]), renal complications (3.4% vs 5.0%), and respiratory complications (4.6% vs 5.3%[13]) were also very similar to previous trials. It is important to note that these comparisons are presented for context only, because event definitions and reporting measures were not the same across the different device trials.

Procedural observations demonstrated the average duration of procedure is approximately one-half of an hour shorter than in earlier TEVAR trials,[2,13,34] which could be a reflection of ease of use of the new device or increased operator familiarity over time for TEVAR in general. As described, there were notable geographical differences with percutaneous access comprising 71.2% of U.S. procedures, whereas 80.0% of OUS procedures were surgical cut downs. Although surgical cut down access was historically thought to be the safer method, existing literature has conflicting results with some studies showing no difference in outcomes based on percutaneous or cut down access and others reporting better results with the percutaneous approach.[35-37] The estimated blood loss was higher in the OUS cohort, as could be expected from the higher percentage of surgical cut downs. However, the overall estimated blood loss in this trial (94.0 ± 147.1 mL) is nearly one-third of what was reported for the previous generation system in the Valor II trial (277.0 ± 468.8 mL)[2] and one-half of the 216 ± 293 mL of another contemporary device.[34]

Interestingly, 47 of 52 U.S. patients (90.4%) had an ICU stay after the index procedure compared with only 16 of 35 OUS patients (45.7%). This difference was likely due to the higher frequency of CSF drainage in the U.S. patients (23.1% [12/52] U.S. vs 8.6% [3/35] OUS) and geographical differences in postprocedural standard of care pathways. For context, the overall frequency of CSF drainage in the Valiant Evo trial is lower than other stent trials, which ranged from 25.6% to 36.4%.[12,34] The median radiation exposure was higher in the U.S. compared with OUS cases, but whether this finding was due to differences in types of adjunctive procedures or the use of different imaging modalities and strategies[38] is beyond the scope of these trials. The radiation exposure of the Valiant Evo patients as a whole is similar to the 0.8 Gy levels reported by Howells et al[39] and in other TEVAR experiences.[38] Further investigations into the regional differences is warranted to assess if certain management strategies may lead to better patient outcomes.

Limitations. As with any single-arm trial, there is no control group and so previously published results of other TEVAR devices are discussed. Comparisons of results with the other trials must be taken in context because patient cohorts, aneurysm characteristics, and outcome definitions likely differed between studies. Additionally, although clinical trials provide more control over patient monitoring and follow-up, the overall

number of patients in the trials was small and the population was more carefully selected than a real-world population. For example, the proportion of women in this trial is greater than that reported in other TEVAR registries and so care must be taken when generalizing these results. Finally, although these acute results were positive, longer term follow-up is necessary to validate the device performance and overall durability of this stent graft system for the treatment of DTAAs and PAUs.

CONCLUSIONS

In this report of short-term outcomes from the Valiant Evo clinical trials for DTAA/PAUs, the primary end point was achieved because only 2 of the 87 patients (2.3%) experienced a MDE within the first 30 days. Despite the challenging anatomic characteristics of the cohort, the low-profile delivery system had no incidences of access artery or deployment failures. The incidence of secondary procedures, endoleaks, and other adverse events were low. With encouraging 30-day results, the Valiant Evo population will continue to be followed through 5 years to assess the long-term durability and performance of the device.

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AUTHOR CONTRIBUTIONS

Conception and design: AA, JP, FV
Analysis and interpretation: AA, ND, FA, JP, FT, PH, FD, LL, FV
Data collection: LL
Writing the article: AA, FV
Critical revision of the article: AA, ND, FA, JP, FT, PH, FD, LL, FV
Final approval of the article: AA, ND, FA, JP, FT, PH, FD, LL, FV
Statistical analysis: LL
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APPENDIX (online only).

Inclusion criteria.

1. Subject was ≥18 years old.
2. Subject understood and voluntarily signed and dated the informed consent form approved by the sponsor and by the ethics committee/institutional review board for this study.
3. Subject presented a descending thoracic aortic aneurysm that was localized below the ostium of the left subclavian artery (LSA) and above the ostium of celiac trunk.
4. Subject had a descending thoracic aortic aneurysm that was one of the following:
   a. A fusiform aneurysm with a maximum diameter that:
      i. was 50 mm or greater; and/or
      ii. was more than two times the diameter of the non-aneurysmal thoracic aorta; and/or
      iii. was less than 50 mm and had grown 5 mm or more within previous 12 months.
   b. A saccular aneurysm or a penetrating atherosclerotic ulcer.
5. Subject's anatomy met all the following anatomical criteria as demonstrated on contrast-enhanced computed tomography and/or on contrast-enhanced magnetic resonance angiography obtained within 4 months before the implant procedure:
   a. Proximal and distal nonaneurysmal aortic neck diameter measurements were 16 mm or greater and 42 mm or smaller.
   b. Proximal nonaneurysmal aortic neck length was greater than 20 mm (for FreeFlo configuration) and 25 mm or greater (for a closed web configuration) distal to the left common carotid artery. Note: The proximal aortic neck length may include covering the LSA (with or without discretionary revascularization) when necessary to optimize device fixation and maximize aortic neck length. If occlusion of the LSA ostium was required to obtain adequate neck length for fixation and sealing, transposition or bypass to the LSA may have been warranted.
   c. Distal nonaneurysmal aortic neck length was 20 mm or greater.
6. Subject had adequate arterial access site or could tolerate a conduit that allowed endovascular access to the aneurysmal site with the delivery system of the appropriate sized device chosen for the treatment.

Exclusion criteria.

1. Subject had a life expectancy of less than 1 year.
2. Participant was participating in another investigational drug or device study that would interfere with the endpoints and follow-ups of this study.
3. Participant was pregnant.
4. Participant required planned placement of the covered proximal end of the stent graft to occur in zones 0 or 1.
5. Participant had a thoracic aneurysm with a contained rupture or localized at the anastomosis of a previous graft (pseudoaneurysm or false aneurysm).
6. Participant had a mycotic aneurysm.
7. Participant had a dissection (type A or B) or an intramural hematoma or an aortic rupture in addition to the thoracic aneurysm.
8. Participant required emergent aneurysm treatment, for example, trauma or rupture.
9. Participant had received a previous stent or stent graft or previous surgical repair in the ascending and/or descending thoracic aorta, and/or in the aortic arch.
10. Participant required surgical or endovascular treatment of an infra-renal aneurysm at the time of implant.
11. Participant had previous surgical or endovascular treatment of an infrarenal aortic aneurysm.
12. Treatment with the Valiant Evo Thoracic Stent Graft would require intentional revascularization of the brachiocephalic artery or the left common carotid artery or the celiac trunk.
13. Participant had or planned to have a major surgical or interventional procedure within 30 days before or 30 days after the planned implantation of the Valiant Evo Thoracic Stent Graft. This exclusion does not include planned procedures that are needed for the safe and effective placement of the stent graft (ie, carotid/subclavian transposition, carotid/subclavian bypass procedure).
14. Participant had a significant and/or circumferential aortic mural thrombus at either the proximal or distal attachment sites that could compromise fixation and seal of the implanted stent graft.
15. Participant had a connective tissue disease (eg, Marfan syndrome, aortic medial degeneration).
16. Participant had a bleeding diathesis or coagulopathy, or refused blood transfusion.
17. Participant had a myocardial infarction within 3 months of the procedure.
18. Participant had a cerebrovascular accident within 3 months of the procedure.
19. Participant had a known allergy or intolerance to the device materials.
20. Participant had a known allergy to anesthetic drugs.
21. Participant had a known hypersensitivity or contraindication to anticoagulants, or contrast media, which is not amenable to pretreatment.
22. Participant had an active or systemic infection at the time of the index procedure.