Endologix LLC

Ovation Abdominal Stent Graft System Platform (Ovation, Ovation Prime, Ovation iX)

Alto Abdominal Stent Graft System

2022 Annual Clinical Update

P120006/R043

04 October 2022

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I. Overview

This annual clinical update provides a review of the ongoing experience with the Ovation Platform and Alto Abdominal Stent Graft System used in the treatment of abdominal aortic aneurysms.

The Ovation PMA (P120006) was approved on October 5, 2012 with subsequent approvals for Ovation Prime (P120006/S001), Ovation iX (P120006/S015, P120006/S020), and the Alto Abdominal Stent Graft System (P120006/S031). The Alto System represents the latest iteration of the Ovation platform and is the only iteration currently manufactured/commercialized by Endologix LLC as of the date of this report. (Summary of Safety and Effectiveness, Instructions For Use).

In this update, 10 years of IDE clinical data, 6 1/2 years of Post Approval Study (PAS) data, and 10 years of worldwide commercial experience is presented. This update contains information that has become available since the reporting period of the last Annual Clinical Update (P120006/R036) up to July 31, 2022[1].

II. Worldwide Device Distribution

Please reference **Table 1** below for a summary of Worldwide Commercial Distribution of Ovation Platform and Alto Implantable Devices.

Table 1 Summary of Worldwide Commercial Distribution of the Ovation Platform*

Device	01 August 2020 – 31 July 2022	Total Lifetime Sales
Ovation Aortic Body	0	1,685
Ovation Iliac Limbs/ Extensions	0	5,116
Ovation Prime Aortic Body	0	8,715
Ovation Prime Iliac Limbs/ Extensions	0	19,903
Ovation iX Aortic Body	453	13,506
Ovation iX Iliac Limbs	13,082	44,606
Ovation iX Iliac Extensions	1,615	6,031
Alto Aortic Body	4,765	4,769
TOTAL	19,915	104,331

**The Ovation Abdominal Stent Graft System, Ovation Prime Abdominal Stent Graft System, Ovation iX Abdominal Stent Graft System, Fill Polymer Kit, and Autoinjector are no longer commercialized. As of the date of this report, the Alto Abdominal Stent Graft System (Alto Aortic Body Stent Graft, Ovation iX Iliac Limb/Extension Stent Grafts, CustomSeal Kit and Autoinjector 2) is the only currently commercial platform iteration in the US and OUS. The Ovation iX Abdominal Stent Graft System was discontinued in the United States on October 31, 2020. Ovation iX was still commercial in certain OUS geographies during the reporting period, but has since been discontinued.*

[1] The data cutoff for the 2022 Annual Clinical Update (ACU) is July 31, 2022, with exception of the JAGUAR study, which includes information to 02 August 2022. This cutoff date is aligned with the data presented in the JAGUAR 30-month report (P120006/R042), acknowledged by FDA on September 23, 2022.

III. Clinical Evaluations

a. Ovation Abdominal Stent Graft System Platform

Ovation IDE Study: Endologix successfully completed the Ovation IDE study in May 2018 which is reported in the Ovation IFU.

https://www.accessdata.fda.gov/cdrh_docs/pdf12/p120006c.pdf

Ovation / Ovation Post Approval Study (PAS): A prospective, consecutively enrolling, single arm multicenter study was initiated to evaluate the long-term safety and effectiveness of the Ovation/Ovation Prime Abdominal Stent Graft System for the endovascular treatment of infrarenal abdominal aortic aneurysms in a commercial environment. The primary study endpoint was freedom from aneurysm-related mortality at five (5) years compared to a performance goal. Key secondary endpoints at 30 days, 12 months, and annually thereafter to 5 years included

- Serious Adverse Events (SAEs). All-cause mortality, AAA-related mortality, device patency, conversion to open surgical repair, endoleak, AAA enlargement, stent graft migration, device integrity, secondary endovascular procedures, and aneurysm rupture.

A total of 320 patients (161 (pivotal), 77 (continued access), and 82 (*de novo*) were enrolled from November 2009 to July 2015. All pivotal, continued access, and *de novo* patients have exited the Ovation PAS as of 20 September 2020. Reference the Ovation / Ovation Prime PAS FDA webpage:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=489523&c_id=770

Results of Ovation Post-Approval Study:
Final close out visits have concluded with a data extraction date of 18 January 2021. Core Lab and site reported data from Ovation/ Ovation Prime Post-Approval Study subjects from 31 July 2015 to 18 January 2021 is shown **Table 2** below:

Table 2 Summary of Final Close Out Data from Ovation PAS subjects from 31 July 2015 to 18 January 2021

		Pivotal Cohort ***x/y****	**Continued Access Cohort** ***x/y****	***De novo* Cohort** ***x/y****	**Total** ***x/y****
Aneurysm Related Mortality		3/161 (1.9%)	0/77 (0.0%)	0/82 (0.0%)	3/320 (0.9%)
All- Cause Mortality		35/161 (21.7%)	17/77 (22.1%)	15/82 (18.3%)	67/320 (20.9%)
Aneurysm Rupture		1/161 (0.6%)	1/77 (1.3%)	0/82 (0.0%)	2/320 (0.6%)
Surgical Conversion		0/161 (0.0%)	0/77 (0.0%)	1/82 (1.2%)	1/320 (0.3%)
All Type Endoleaks:	**Type IA**	0/157 (0.0%)	0/75 (0.0%)	2/77 (2.6%)	2/309 (0.6%)
	Type IB	0/157 (0.0%)	0/75 (0.0%)	1/77 (1.3%)	1/309 (0.3%)

	Type II	77/157 (49.0%)	36/75 (48.0%)	29/77 (37.7%)	142/309 (46.0%)
	Type IIIA	0/157 (0.0%)	0/75 (0.0%)	1/77 (1.3%)	1/309 (0.3%)
	Type IIIB	0/157 (0.0%)	0/75 (0.0%)	0/77 (0.0%)	0/309 (0.0%)
	Type IV	0/157 (0.0%)	0/75 (0.0%)	0/77 (0.0%)	0/309 (0.0%)
	Indeterminate Origin	22/157 (14.0%)	11/75 (14.7%)	5/77 (6.5%)	38/309 (12.3%)
Aneurysm Enlargement > 5 mm	22/153 (14.4%)	7/69 (10.1%)	12/65 (23.1%)	41/287 (14.3%)	**Aneurysm Enlargement > 5 mm**
Stent Graft Migration	0/156 (0.0%)	0/70 (0.0%)	0/78 (0.0%)	0/304 (0.0%)	**Stent Graft Migration**
Loss of Device Patency (Occlusion)	4/159 (2.5%)	2/76 (2.6%)	5/76 (6.6%)	11/311 (3.5%)	**Loss of Device Patency (Occlusion)**
AAA-related Secondary Procedures	33/161 (20.5%)	20/77 (26.0%)	7/82 (8.5%)	60/320 (18.8%)	**AAA- related Secondary Procedures**
Loss of Device Integrity**	11/161 (6.80%)	6/77 (7.80%)	3/82 (3.70%)	20/320 (6.30%)	**Loss of Device Integrity****

**x is the number of subjects who reported that event, and y is the number of subjects with follow-up/adequate imaging to assess the parameter.*
***The device integrity information came from Core Lab reviewed x-rays among the Pivotal and Continued Access cohorts, and was site reported for the De novo subjects.*

- One surgical conversion, due to aneurysm enlargement was reported under the post-approval study.

- With respect to secondary interventions, the subjects with stenosis or occlusion were treated with stenting, balloon angioplasty, thrombolysis, and/or thrombectomy, and four subjects were treated with a fem-fem bypass (one after an unsuccessful thrombectomy). One Continued Access subject had a resulting hematoma that required additional treatment. The other subjects have had no additional re-interventions or clinical sequelae reported after the secondary procedure.

- In total, there were 20 subjects that had Loss of Device Integrity (LDI). Among the 20 subjects, 17 had LDI due to stent fractures in the proximal stent graft. A total of 15 were single wire fractures and 2 were double wire fractures. A review of the images for the 17 subjects showed no movement of the device or collapse of the stent cage. The remaining 3 subjects had LDI due to compression/deformity of the stent. There were no associated clinical sequelae reported with these events and no device-related interventions resulted from these events. The 3 subjects with compression/deformity of the stent were described as "mild aortic graft compression", "slight compression of proximal endograft/compression distal aortic graft body", and "deformity in stent secondary to incomplete stent (expansion); proximal portion".

b. Alto Abdominal Stent Graft System Platform

Alto IDE (ELEVATE) IDE Study: Endologix successfully completed the Alto IDE study in March 2019 which is reported in the Alto IFU.
https://www.accessdata.fda.gov/cdrh_docs/pdf12/P120006S031C.pdf

Alto Case Selection and Sizing Study (CSSS): A multi-center clinical evaluation was initiated to compare physician selection of patients for the Alto device compared with Endologix Imaging Services using the same diagnostic, de-identified, CT Scan in 100 subjects. The study endpoints include a description of any differences and concordance with respect to key anatomic measurements for Alto device sizing, general suitability for EVAR, compliance with the anatomic indications for use, and Alto Aortic Body size selected. Sites began enrolling subjects for the CSSS on 30 July 2020 and completed enrollment (n=100) on 22 December 2020. The 30-day post implant timepoint was reached for all subjects with the final subject's 30-day timepoint occurring on 21 January 2021. Reference the Alto CSSS PAS on FDA webpage:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=662675&c_id=6009

For the 100 subjects enrolled, there has been 100% agreement and 0% disagreement among physician users and Endologix Imaging Services with respect to Alto Aortic Body sizing recommendations and suitability for EVAR.

Alto US and OUS Post-Approval Study (JAGUAR Trial): A prospective, randomized, multi-center US and OUS Post-Approval Study was initiated to collect safety, effectiveness, and neck dilatation data on the Alto Abdominal Stent Graft System and evaluate real world outcomes in comparison to commercially available comparator devices. There are two primary endpoints: a clinical endpoint and a surrogate. The clinical endpoint is a composite of aneurysm-related complications (ARC) and consists of freedom from device-related interventions (for Type I & III endoleaks, stenosis/occlusion, migration, or other device- related cause), conversion to open surgery, Type I and III endoleaks, device migration (>10 mm), aneurysm sac enlargement (>5 mm), occlusion, aneurysm rupture, and aneurysm-related death. The surrogate endpoint is the hypothesized physiologic mechanism that leads to failure of several components within the clinical endpoint: proximal neck dilation over time. The surrogate allows for an early insight into eventual clinical sequelae. All individual components of the primary endpoint will be evaluated as separate outcomes using the Kaplan-Meier approach. Results will be stratified by device cohort. A minimum of 450 consented patients diagnosed with AAA who are considered candidates for endovascular repair and meet the study eligibility criteria, will be randomized. At least 300 will be allocated to the Alto cohort, and 150 to the comparator group.

The first subject was enrolled for the US and OUS PAS on 20 September 2021. As of 02 August 2022, 36 subjects had been implanted in the JAGUAR Trial. As the study is still in the early stages of enrollment, no conclusions can be drawn at this time.

Reference the Alto RCT (Randomized Controlled Trial) US and OUS PAS on FDA webpage: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=662675&c_id=6010.

IV. Worldwide Recalls, Safety Communications and Field Safety Notices

This section does not include information for the Ovation and Ovation Prime Abdominal Stent Graft Systems as they are no longer manufactured or marketed.

The Ovation iX Abdominal Stent Graft System is also no longer manufactured or commercialized by Endologix. However, the Ovation iX Aortic Body Stent Graft and Autoinjector were still sold outside of U.S. during the reporting period, therefore safety communications for the Ovation iX System are included in this report.

From the time of commercial launch through 31 July 2022, there have been two safety communications regarding the Ovation iX Abdominal Stent Graft System which are summarized below.

- On 06 August 2018 Endologix issued communication to physician users due to an increase in intra-operative polymer leaks identified with the Ovation iX Abdominal Stent Graft System compared to historical levels. (https://endologix.com/wp-content/uploads/2018/08/Ovation-FSN-Aug-06-Final.pdf) The polymer leaks resulted in death (AAA-related); multi-organ failure/cardiac arrest/neurological complication; local tissue necrosis; prolonged hemodynamic instability, and transient hemodynamic instability.

Investigation determined that most polymer leaks resulted from deviations to the procedural sequence related to the polymer fill and procedural steps provided in the IFU. The purpose of the safety communication was to emphasize the importance of following the polymer fill procedural sequence as instructed and provide information specifically regarding: 1) Patient Reaction; 2) Aneurysm Management; 3) Procedural Considerations; and 4) Warnings and Cautions. No changes to the IFU were required.

- On 06 May 2020, Endologix issued a communication to physician users of the Ovation iX Abdominal Stent Graft System to provide a safety update regarding polymer leaks during implantation. (https://endologix.com/wp-content/uploads/2020/05/ENDO-Ovation-FSN-FS-0012-US-Letter-Final-5-6-20.pdf) This safety update reaffirmed treatment recommendations for patients who experience a polymer leak during implantation and provided updated information on the current rate of polymer leaks, the rate of clinical harms and the root cause. FDA identified this as a Class I recall. (https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm?id=181049)

The investigation determined that technical and procedural factors of the user (e.g. use of the cross over lumen before polymer fill, catheter manipulation) are not causative for the majority of polymer leaks, as was previously communicated. Adherence to the procedural steps within the Instructions for Use continues to be recommended and are not modified in this safety update. The root cause for most polymer leaks was determined to be a material weakness adjacent to the polymer fill channel which may become compromised during pressurization with liquid polymer.

The following was included as a part of Field Safety Notice as further risk mitigations for intravascular leak of polymer:

- Promptly treating the patient for potential severe hypersensitivity reaction if a polymer leak is identified
- Adhering to the procedural steps in the published device instructions for use (IFU) including existing IFU Caution and Warning statements and avoiding excessive device manipulation.

Endologix transitioned the US market completely from Ovation iX to the Alto Abdominal Stent Graft System at the end of October 2020. Alto incorporates design and manufacturing changes that are intended to eliminate the areas of material weakness associated with polymer leaks. Additionally, in an effort to mitigate the procedural polymer leak risk, Endologix is committed to the Alto Physician Training Program which incorporates best practices for polymer management. In accordance with our quality system and post-market surveillance procedures, Endologix will continue to closely monitor Alto device performance, including any instances of polymer leak. As of the date of this report, Alto is the only iteration of the Ovation Platform which is manufactured or distributed by Endologix.

There have been no safety communications regarding the Alto Abdominal Stent Graft System since commercialization in July of 2020.

V. Worldwide Commercial Experience

As part of continuous monitoring of Ovation iX lifetime device performance, the most common global product complaint category from commercialization to the current data cut (08 August 2015 – 31 July 2022) was Type IA endoleak. During this time period there were 327 Type IA events that occurred out of a total of 13,506 devices sold [327/13,506], which equals a rate of 2.42%. The root cause analysis identified that the majority of Type IA endoleaks are acute (<30 days) and the variables associated with Type IA endoleaks include the anatomical variances of reverse taper neck and juxtarenal angle. Global Medical Affairs continues to conduct procedural training globally to all certified Ovation case supporters through a series of webinars, online modules and assessments.

The top five global product complaint categories, when a Type IA endoleak is present, are: additional endovascular procedure [114/13,506], rate=0.84%; type II endoleak [48/13,506], rate=0.36%; aneurysm enlargement [35/13,506], rate=0.26%; transient hypotension [31/13,506], rate=0.23%; and aneurysm not excluded [20/13,506], rate=0.15%.

Likewise, as part of continuous monitoring of Alto lifetime device performance, the most common global product complaint category from commercialization to the current data cut (22 July 2020 – 31 July 2022) was Type IA endoleak. During this time period there were 46 Type IA events that occurred out of a total of 4,769 devices sold [46/4,769], which equals a rate of 0.96%. The root cause analysis identified that the majority of Type IA endoleaks are associated with patient anatomy, cautionary product use, and indeterminate.

The top five global product complaint categories of Alto, when a Type IA endoleak is present, are: type II endoleak [11/4,769], rate=0.23%; additional endovascular procedure [10/4,769], rate=0.21%; death (AAA related) [3/4,769], rate =0.06%; rupture (aorta) [3/4,769], rate=0.06%; cardiac arrest and hemodynamic instability both have [2/4,769], rate=0.04%.

Endologix will continue to closely monitor Ovation and Alto device performance, including Type IA endoleak trend.

VI. Explant Analysis

Endologix monitors product performance to ensure the ongoing quality, safety, and efficacy of its products. Upon explant and return of a product, a historical review, engineering evaluation, and histopathological evaluations of explanted stent grafts are performed.

Since the launch of Alto through 31 July 2022, there were six (6) Alto explants out of a total of 4769 implant procedures worldwide (0.13%), as compared with a cumulative lifetime rate of 0.26% for the previous Ovation iX platform. See **Table 3** below for a summary of these explants.

Table 3 Summary of Alto Explants

Patient ID	Date of Implant procedure	Date of Explant	Event Description
52783	19 May 2021	19 May 2021	The patient was initially treated for an abdominal aortic aneurysm (AAA) with one Alto Main Body and two Ovation iX Iliac Limbs. During the initial implant, a type Ia endoleak was noted at final angiogram. The physician elected to treat the patient by utilizing a non-Endologix balloon (Coda). However, the patient was observed to have hypotension, then went into cardiac arrest. CPR was performed and the patient stabilized. An aortic rupture was suspected, therefore the physician elected to implant a GORE EXCLUDER (non-Endologix) cuff. During deployment of the cuff, the Coda balloon was removed, at which time the patient arrested again. The physician then elected to convert patient to open surgery and the Alto device was explanted and replaced with a Gelsoft Plus (non-Endologix) prosthesis. The patient then deceased within 48-hours of the index procedure. The explanted devices are not available for return/evaluation despite requests by the manufacturer, and the causal relationship of the incident could not be determined due to insufficient information.
56188	2 February 2022	10 February 2022	The patient was implanted with the Alto Stent Graft system to treat an abdominal aortic aneurysm (AAA). During this initial procedure, the main body was implanted with the limbs in a crossed configuration due to tortuous anatomy. The physician rotated the image to visualize the contralateral gate and proceeded to cannulate. Gate cannulation was confirmed visually and also a pigtail catheter was advanced over a wire which was then spun to confirm cannulation. Both iliac limbs were deployed and proceeded with the final angiogram which showed the aneurysm was still filling and not excluded. A type 1 endoleak was excluded. The image was rotated to extreme to left anterior oblique (LAO) and it was discovered both

			limbs were placed in the ipsilateral side. The patient had blood flow to the extremities and was stable when closed. Eight (8) days post initial procedure, the physician elected to partially explant the main body stent graft. The proximal crown and the iliac limbs remained in the patient. The physician then Implanted a tube graft from the proximal crown to the limbs in iliac arteries. The explanted aortic body was retained by the user facility and later discarded. The patient was reported as doing well post the explant procedure.
57214	3 May 2022	3 May 2022	The patient was implanted with the Alto Stent Graft system to treat an abdominal aortic aneurysm (AAA). It was reported that before implant of the Alto stent graft system, the right iliac artery was dissected and this was the same side where the delivery system was inserted. During this initial procedure, the polymer started filling; however, only a small amount entered the device and it stopped filling. The remainder of the polymer remained in the syringe. The physician manipulated the delivery system in attempts to fill the polymer but was unsuccessful. After 14 minutes had elapsed additional attempts were made to access the polymer channel with wires and a catheter and in the meantime the patient's blood pressure decreased to 70 mmHg. The physician elected to remove the delivery system and to explant the device cutting it below the suprarenal stent and to implant a surgical protheses. After the open surgery the patient was sent to intensive care. Although a conclusion has yet to be established as the investigation is incomplete, analysis of the incident noted possible excessive manipulation of the delivery system. In addition, there was thickened circumferential calcifications in the distal right common iliac artery, with a conicity of 20.4% (vs IFU requirement of <10%), which might have contributed to iliac dissection.
57264	6 May 2022	6 May 2022	The patient was initially treated for an abdominal aortic aneurysm (AAA) with implant of the Alto Main Body. During the initial implant procedure, the physician experienced difficulty orientating the delivery system as the radiopaque markers were reportedly not well aligned. The physician then noted slight resistance while inflating the integrated balloon during mid-crown deployment of the Main Body. In addition, physician was unable to deflate the integrated balloon, which resulted in converting patient to open repair. The patient was then transferred to ICU. Patient was in good condition and discharged from hospital. No relevant medical records nor medical imaging was received by Endologix after repeated attempts to collect. As such, a clinical evaluation of the incident could not be completed,

			and the causal relationship of the incident could not be determined.
58169	27 May 2022	19 July 2022	Approximately 7 weeks following implantation, the patient was transferred to the hospital for suspected graft infection. The patient was treated with antibiotics and the stent graft was explanted and a conventional aortic graft was sewn in. The inferior mesenteric artery and lumbars were patent and there was no type 1 or 3 leak. Patient did well after surgery.
57906	20 June 2022	20 June 2022	The patient was being implanted with the Alto Stent Graft system to treat an abdominal aortic aneurysm (AAA). It was reported that during the procedure, the physician forwarded the device further than was intended (approximately 4-5cm above the planned landing spot). An attempt was made in the hopes that the barbs on the supra-renal stent had not engaged the aorta, but was unsuccessful. The procedure was stopped and a surgeon was called to successfully removed the graft. The final patient status was reported as being stable and taken to ICU.

VII. Literature Review

The current systematic review of the literature from 01 July 2021 to 30 April 2022 identified a total of 9 review articles on State-of-the-Art of the device. There were no device specific articles providing clinical safety/performance outcomes on the Ovation Platform and Alto Abdominal Stent.

VIII. Conclusion

Based on available clinical study data and world-wide clinical experience to date, endovascular therapy with the currently marketed Alto Abdominal Stent Graft System continues to be a viable treatment option for abdominal aortic aneurysms.

Adverse Event Reporting:

Any adverse event involving the Ovation or Alto devices should be reported immediately to the Endologix Customer Service Department at 800-983-2284 (24 hours message service). Outside the U.S., contact your local Endologix representative. Accurate and timely reporting of adverse events by the physician users to the device manufacturer and FDA (MedWatch Form 3500) is critical for monitoring device performance and detection of potential device-related safety issues.

Patient Follow-Up and Selection:

Regular follow-up of all patients treated with the Ovation and Alto Abdominal Stent Graft Systems is required. Physicians should tailor follow-up to the needs and circumstances of each individual patient.