SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Iliac Covered Stent, Arterial
Device Trade Name:	iCast™ Covered Stent System
Device Procode:	PRL
Applicant's Name and Address:	Atrium Medical Corporation 40 Continental Blvd Merrimack, NH 03054
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P120003
Date of FDA Notice of Approval:	March 22, 2023

II. INDICATIONS FOR USE

The iCast Covered Stent System is indicated for improving luminal diameter in patients with symptomatic atherosclerotic disease of the native common and/or external iliac arteries up to 110 mm in length, with a reference vessel diameter of 5 to 10 mm.

III. CONTRAINDICATIONS

The iCast Covered Stent System is contraindicated for use in:

- Patients with uncorrected bleeding disorders.
- Patients who cannot receive recommended antiplatelet and/or anticoagulation therapy.
- Patients who are judged to have a lesion that prevents full expansion of the implant.
- Lesions in which the lumen diameter post-balloon angioplasty is insufficient for the passage of the endovascular system.
- Lesion locations subject to external compression.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the iCast Covered Stent System labeling.

V. DEVICE DESCRIPTION

The iCast Covered Stent System consists of a balloon expandable ePTFE covered stent and an over-the-wire (OTW) delivery system. The iCast Covered Stent consists of a laser cut 316L stainless steel stent encapsulated in expanded PTFE. The stent is crimped onto an OTW balloon

dilatation delivery catheter. The device is available in diameters of 5mm to 10mm and crimped lengths of 16mm, 22mm, 38mm, and 59mm. See Table 1 below.

The OTW delivery catheter has a wire lumen that is used for flushing and guidewire introduction. The delivery system is compatible with a 0.035" guidewire and has a useable length of 80cm or 120cm. The secondary or inflation lumen(s) are used for inflation/deflation of the attached balloon to deploy the endoprosthesis. To facilitate accurate device placement, two radiopaque bands are attached to the catheter shaft marking the ends of the crimped device and dilatation length of the balloon. See Figure 1 below.

Table 1: iCast Stent Sizes

Diameter (mm)	**Length (mm) unexpanded**			
	16	22	38	59
5	√	√	√	√
6	√	√	√	√
7	√	√	√	√
8	-	-	√	√
9	-	-	√	√
10	-	-	√	-
Note that the entire iCast Stent matrix is available in both 80 cm and 120 cm catheter lengths.				

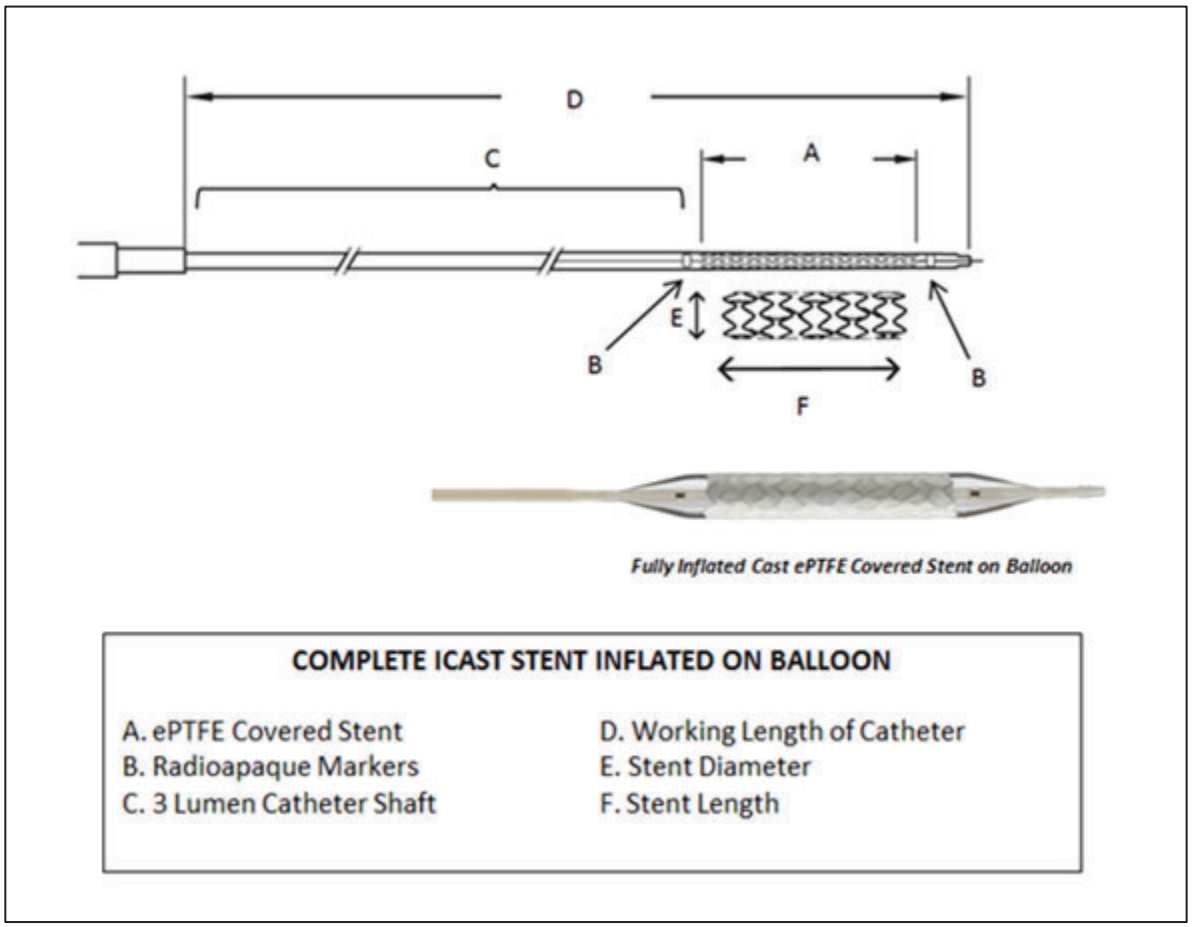

Figure 1: iCast Stent System

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of iliac atherosclerotic disease:

- Non-invasive treatment (e.g., exercise, smoking cessation and/or drug therapy);
- Minimally invasive treatment (e.g., balloon angioplasty, endovascular stent or stent-graft placement, directional atherectomy, mechanical thrombectomy); and
- Surgical treatment (e.g., surgical bypass).

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The iCast Covered Stent has been marketed outside the U.S. under the name of Advanta V12 PTFE Covered Stent since 2002. The product has been marketed for iliac artery use in the following countries listed below in Table 2. Since commercialization, the iCast/Advanta V12 Covered Stent has not been withdrawn from the market for any reason.

Table 2: iCast Covered Stent System Marketing Approvals (marketed outside the U.S. under the name of Advanta V12 PTFE Covered Stent)

Albania	Dominican Republic	Italy	Panama	Switzerland
Argentina	Ecuador	Jordan	Peru	Taiwan
Australia	Egypt	Kuwait	Poland	Thailand
Austria	El Salvador	Latvia	Portugal	Turkey
Belgium	Estonia	Lebanon	Qatar	United Arab Emirates
Bolivia	Finland	Lithuania	Romania	United Kingdom
Brazil	France	Luxembourg	Russia	Uruguay
Bulgaria	Germany	Malaysia	Saudi Arabia	
Canada	Greece	Malta	Singapore	
Chile	Honduras	Mauritius	Slovakia	
Colombia	Hong Kong	Mexico	Slovenia	
Costa Rica	Hungary	Netherlands	South Africa	
Cyprus	Iceland	New Zealand	South Korea	
Czech Republic	Ireland	Norway	Spain	
Denmark	Israel	Pakistan	Sweden	

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the probable adverse effects (e.g., complications) associated with the use of the device:

- Acute myocardial infarction
- Allergic reaction to stainless steel, PTFE, drugs or contrast agent
- Angina/coronary ischemia
- Arrhythmia
- Arterial aneurysm
- Arterial rupture
- Arteriovenous fistula
- Bleeding complications from anticoagulant or antiplatelet medication requiring transfusion or surgical intervention
- Death
- Detachment, dislodgement, and/or implantation of a component of the system
- Emboli (air, tissue, or thrombotic emboli)
- Emergency surgery to correct vascular complications
- Hematoma/hemorrhage
- Hypotension/hypertension
- Infection, local or systemic
- Intimal injury/dissection/perforation
- Pain at catheter insertion site or limb
- Pseudoaneurysm formation
- Pulmonary embolism
- Renal insufficiency or failure

- Restenosis of the stented artery/occlusion
- Short-term hemodynamic deterioration
- Stent malposition/stent migration
- Stent strut fracture
- Stent thrombosis/occlusion
- Stroke
- Target limb loss (amputation of toe, foot and/or leg)
- Tissue necrosis
- Vascular thrombosis
- Vessel spasm
- Worsening claudication/rest pain

For the specific adverse events that occurred in the clinical studies, please see Sections X and XI below.

IX. SUMMARY OF NONCLINICAL STUDIES

A. *Laboratory Studies*

In vitro bench testing to support the safety and effectiveness of the iCast™ Covered Stent was developed based on Atrium Medical's Product Development Process and is consistent with the FDA Guidance, *Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, April 18, 2010* and *ISO 25539-1:2009 Cardiovascular implants -- Endovascular devices -- Part 1: Endovascular prostheses*. The relevant *in vitro* tests, outlined in the guidance document, and conducted to support the iCast™ Covered Stent are summarized in Table 3. All test units were ethylene oxide sterilized prior to testing, unless otherwise noted in the test report.

Table 3: Summary of *In Vitro* Bench Testing

***In Vitro* test**	**Purpose**	**Acceptance Criteria**	**Results**
Material Characterization			
Material Composition Stent	To verify chemical composition of the implant.	Material composition must comply with ASTM F138-13.	PASS
Corrosion Resistance	To verify the implant's ability to resist corrosion (fretting, pitting and crevice corrosion).	Fretting Corrosion: No presence of fretting corrosion with visual examination using a digital microscope and/or Scanning Electron Microscope (SEM) for stent samples fatigue tested in an overlapped condition. Pitting and Crevice Corrosion: Materials tested per ASTM F2129-06 must meet the following breakdown potential: Eb ≥ +600mV Or if Eb < +600mV, then	PASS

In Vitro test	Purpose	Acceptance Criteria	Results
		Eb ≥ +300mV and Eb – Er ≥ +200mV where Eb - Er is a measure of the difference between the breakdown potential Eb and the resting potential Er.	
Stent Dimensional and Functional Attributes			
Dimensional Verification	To verify that critical implant dimensions (implant outer diameter and length in the unconstrained expanded condition) are met.	5, 6, 7, 8, 9 and 10 mm implant outer diameter 16, 22, 38 and 59 mm implant length	PASS
Foreshortening	To quantify the percent change in length of the implant from between its crimped and deployed states.	The percentage of foreshortening must be ≤26%.	PASS
Diameter and Recoil	To quantify the percent decrease in diameter of the implant from between its deployed and relaxed states.	The difference in stent diameter at balloon inflation and after balloon deflation should be calculated for each stent. 5-10mm: OD = Labeled balloon diameter ± 10% (following deflation from nominal pressure) Recoil: ≤ 15%	PASS
Stent Integrity	To evaluate the integrity of the stent post-deployment for defects.	Stents should not exhibit cracks, fractures or breaks post expansion.	PASS
Radial Stiffness and Radial Strength	To characterize the ability of the stent to resist collapse under short-term or long-term external loads.	The radial strength of the stent must be able to withstand an external radial pressure loading of ≥ 225mmHg at a diameter reduction of 25% of labeled stent diameter.	PASS
Flex/Kink of Stent Post-Deployment	To evaluate the ability of deployed stent to fit the anatomy without kinking.	Stent does not kink after deployment within target vessel.	PASS
Conformability	To evaluate the ability of the stent to adequately contact the vessel wall upon deployment.	Stent must be apposed to vessel wall after deployment per ISO 25539-1:2009/AC:2011.	PASS
Fixation Effectiveness	To evaluate the ability of the stent to remain in its deployed position.	Stent must be able to remain in position after deployment and become integrated into the vessel wall per ISO 25539-1 :2009/AC:2011.	PASS

In Vitro test	Purpose	Acceptance Criteria	Results
Migration Resistance	To evaluate the ability of the implant to remain stationary under simulated use.	Stent must not migrate from its initial deployment position per ISO 25539-1 :2009/AC:2011.	PASS
Mechanical Properties (Raw Stent Material)	Mechanical properties of raw stent material should be verified.	ASTM F138-13a	PASS
Mechanical Properties (Covered Stent)	To characterize the permeability, Internodal Distance (IND) and Integral Water Permeability (IWP) of the covering and verify they conform to their specification.	WEP must be ≥120mmHg for all samples. IND must be characterized. IWP must be characterized.	Material has been characterized.
Stress/Strain Analysis	To determine maximum stresses and strains within the device.	Strains were calculated using the worst-case configurations in a validated FEA model.	PASS
Fatigue Analysis	To evaluate the durability and integrity of the stent via finite element analysis.	Fatigue Safety Factor ≥ 1.0. All data points on Goodman Diagram for stent at maximum diameter must be below the Goodman Line (Fatigue Safety Factor ≥ 1.0).	PASS
Accelerated Durability	To evaluate the durability and integrity of the stent through 10 years of pulsatile fatigue per ASTM F2477-07.	After 10 years of pulsatile fatigue (minimum 380M cycles): Stents are to be free of all cracks, fractures or breaks using 20X (min.) magnification on optical microscope.	PASS
MRI Safety & Compatibility	To evaluate MRI safety and compatibility.	The stent must demonstrate acceptable MR safety and compatibility per ASTM F2503-20.	PASS
Radiopacity	To evaluate the radiopacity of the stent.	Stent ends should be visible (radiopaque) enough to discern ends of stent in pre-deployed and post-deployed conditions using fluoroscopic imaging equipment.	PASS
Delivery System Dimensional and Functional Attributes			
Dimensional Verification: Delivery System	To verify that the delivery system meets dimensional specifications.	Shaft Usable Length: • 80 +/- 5cm • 120 +/- 5cm The lumen is compatible with a 0.035" guidewire. The catheter can be passed through an appropriately	PASS

In Vitro test	Purpose	Acceptance Criteria	Results
		sized sheath without stent dislodgement. 0.035" guidewire must pass through catheter guidewire lumen.	
Introducer Sheath Compatibility	To verify that the delivery system can be used with commercially available introducer sheaths.	Balloon catheter with stent must pass through sheath/introducer as specified on the product label without stent dislodgment or catheter damage.	PASS
Deployment and Retraction-Post Simulated Use	To ensure that the delivery system meets its pre-determined acceptance criteria with respect to its delivery, deployment, and retraction in a simulated use environment.	Passage over a guidewire through an introducer sheath placed within the specified anatomy without stent dislodgement. Deployment of full stent length between marker bands following passage through introducer sheath over a guidewire within the specified anatomy. Deflated balloon catheter without stent must be able to be withdrawn through specified sheath as indicated on product label.	PASS
Delivery, Trackability, Pushability, Simulated Use	To evaluate the ability of the delivery catheter to deliver the stent to the intended location in a simulated use environment.	In an appropriate simulated use model, the stent system must be able to pass through an introducer sheath, over a guidewire and reliably deliver the stent to the intended location without damage to the stent or balloon catheter, including binding or buckling the catheter.	PASS
System Burst Pressure (RBP)	To evaluate that the delivery system will not experience loss of integrity at or below rated burst pressure.	Burst Pressure ≥ 12 atm (1216 kPa) with 95% confidence and 99.9% reliability.	PASS
Balloon Compliance	To evaluate the covered stent diameter based on balloon inflation pressure to ensure appropriate sizing selection of the covered stent.	Balloon outer diameter must exhibit <10% growth from 8atm to 12atm (nominal to rated burst pressures).	PASS
Balloon Inflation/ Deflation Time	To evaluate the inflation times to RBP and deflation times from RBP.	Inflation: ≤ 30 seconds based on water Deflation (based on water): ≤ 30 sec for 5-8mm ≤ 40 sec for 9-10mm diameters	PASS

In Vitro test	Purpose	Acceptance Criteria		Results
Balloon Fatigue	To evaluate performance of the delivery system balloon and its ability to withstand multiple inflations.	System must not leak when subjected to 10 inflate/deflate cycles at RBP with 30 sec dwell times with 95% confidence and 90% reliability.		PASS
Catheter Bond Strength and Shaft Strength	To evaluate the tensile strengths of the catheter bonds against specifications.	The strength of the proximal balloon weld, manifold to shaft bond and shaft strength of the product must meet or exceed the values in the table below:		PASS
		Tensile Strength of:	Device Size Minimum Tensile Strength	
		Shaft	5-10mm = 15N	
		Manifold Bond	5-10mm = 15N	
		Proximal Balloon Weld	5,6mm x 16, 22mm = 10N 7mm x 16, 22mm = 15N 5-10mm x 38, 59mm = 15N	
Tip Pull Test	To verify the tensile strength of the tip weld meets specifications.	The tip strength of the product must meet or exceed 10N.		PASS
Flex/Kink of System	To verify the ability of the delivery system to withstand flexural forces typical of clinical use during stent delivery.	Device tracks and reaches target while passing through an introducer sheath over a guide wire within simulated anatomy without damage to the delivery system or accessory devices. When the catheter is navigated over a guidewire and when wrapped around a series of descending diametric pins, the catheter must not kink and the lumen must not collapse above a minimum specified diameter (Kink diameter ≤ 20mm).		PASS
Torque Strength	To verify that the delivery system strength can maintain integrity under torsional forces typical of clinical use.	Bonds remain intact and guide wire must be free to move after applying ten rotations to the catheter after its tip has been fixed in an anatomical model.		PASS
Stent Securement for	To evaluate implant retention on the balloon.	Minimum stent retention value after passage through sheath, over the		PASS

In Vitro test	Purpose	Acceptance Criteria	Results
Unsheathed Stents		wire within the simulated anatomy must be ≥ 0.90N Minimum stent retention value upon removal from packaging (out of box) must be: ≥ 2.9N for 6Fr sheath compatible devices ≥ 5.5N for 7Fr sheath compatible devices	

B. Biocompatibility Studies

The biocompatibility of the iCast Covered Stent was evaluated per the requirements of ISO 10993-1:2018 and the FDA Guidance, *Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*. Tests were conducted separately on finished sterile stents and stent delivery systems. All testing was performed in accordance with FDA Good Laboratory Practice (GLP) regulations (21 CFR, Part 58).

The iCast Covered Stent was categorized as an implant device in permanent contact with circulating blood (>30 days), and the delivery system was categorized as an externally communicating device, in limited contact with circulating blood (<24 hours). Table 4 summarizes the biocompatibility testing performed. All test results indicate that the materials and processes used to manufacture the iCast Covered Stent System are biocompatible and suitable for their intended use.

Table 4: Summary of Biocompatibility Test Results for the iCast Covered Stent

Endpoint	Test Performed	Covered Stent	Delivery System	Results
Cytotoxicity	MEM Elution (ISO 10993-5:2009)	X	X	Non-cytotoxic
Sensitization	Guinea Pig Maximization (ISO 10993-10:2010)	X	X	Non-sensitizing
Irritation	Intracutaneous Reactivity (ISO 10993-10:2010)	X	X	Non-irritating
Pyrogenicity	Rabbit Pyrogen—Material Mediated (ISO 10993-11:2017)	X	X	Non-pyrogenic
Acute Systemic Toxicity	Injection Systemic Toxicity (ISO 10993-11:2017)	X	X	Non-toxic

Endpoint	Test Performed	Covered Stent	Delivery System	Results
Sub-chronic and Chronic Systemic Toxicity	4 Week Systemic Toxicity (ISO 10993-11:2017)	X	N/A	Non-toxic
	26 Week Systemic Toxicity (ISO 10993-11:2017)	X	N/A	Non-toxic
Implantation	Muscle Implantation – 6 weeks (ISO 10993-6:2007)	X	N/A	Non-toxic
	Muscle Implantation – 12 weeks (ISO 10993-6:2007)	X	N/A	Non-toxic
Hemocompatibility	Hemolysis (Direct & Indirect) (ISO 10993-4:2017)	X	X	Non-hemolytic
	Complement Activation (ISO 10993-4:2017)	X	X	Not a complement activator
	Thromboresistance (ISO 10993-4:2017)	X	X	Non-thrombogenic
	Partial Thromboplastin Time (ISO 10993-4:2017)	X	N/A	Not an activator of thromboplastin
Genotoxicity	Ames Assay (ISO 10993-3:2014)	X	N/A	Non-mutagenic
	Mouse Lymphoma Assay (ISO 10993-3:2014)	X	N/A	Non-genotoxic
	Mouse Micronucleus (ISO 10993-3:2014)	X	N/A	Non-genotoxic

C. Sterilization, Packaging and Shelf-Life Testing

The iCast Covered Stent is sterilized with ethylene-oxide (EO). The sterility assurance level (SAL) meets a minimum of 10^{-6} as per ANSI/AAMI ST67:2011/(R)2017 *"Sterilization of health care products - Requirements and guidance for selecting a sterility assurance level (SAL) for products labeled 'sterile'."* The sterilization validation was completed in accordance with ANSI/AAMI/ISO 11135:2014 *"Sterilization of health care products — Ethylene oxide — Part 1: Requirements for development, validation, and routine control of a sterilization process for medical devices*". The continued effectiveness of the validated system, in line with ANSI/AAMI/ISO 11135:2014, is demonstrated via routine product bioburden monitoring and periodic reviews of the entire system including equipment, process, and product status. The sterilization studies demonstrate that the product satisfies a minimum SAL of 10^{-6}.

The iCast Covered Stent is packaged individually using a thermoformed PETG clamshell tray which is placed inside a Tyvek® and Mylar pouch which is heat sealed. The sealed pouch is then placed in a chipboard box. Packaging validation testing has been conducted per ISO 11607 on the iCast Covered Stent packaging including visual inspection, and seal strength testing on devices that underwent 3x EO at baseline and following 3-year real-time aging to confirm the integrity of the sterile barrier on aged packaging and seals. Performance testing on the device following 3-years real-time aging supported the 3-year shelf-life. Tests conducted on the packaging and device at shelf life are described in Table 5.

Table 5: Packaging and Shelf-Life Testing

Test Name	Purpose	Acceptance Criteria	Results
Packaging System Visual	To assess legibility of labeling	Labeling is legible	PASS
Sterile Barrier Visual	To assess for the absence of tears or holes in the pouch or other breaches of the seals.	No visual defects observed.	PASS
	To assess for the absence of a continuous channel across the width of the seal.	No seal failures. Seal width must remain greater than 3/16".	PASS
Sterile Barrier Integrity	To assess for the absence of a continuous channel across the width of the seal.	Failure is defined as penetration of the dye solution across the seal width in less than 5 seconds per side.	PASS
Sterile Barrier Strength	To assess for sufficient strength of seals.	Peel Strength ≥ 1.54 lbf/in.	PASS

D. Animal Studies

An *in vivo* study was performed to evaluate the safety of the iCast stent in both single stent and overlapping configurations using a porcine iliac model.

1. Procedure

This study was conducted in accordance with Good Laboratory Practice (GLP) Regulations 21 CFR Part 58. Yorkshire swine were implanted with one 38mm long iCast covered stent in one iliac vessel and one 38mm stent overlapped with a 22mm stent in the contralateral iliac vessel. Six animals were sacrificed at 28 days and six at 90 days following implantation. Following sacrifice the test articles were explanted with the associated vascular tissue for evaluation. Post-implant angiograms were recorded. Evaluation was carried out by gross visualization, morphometry measurements for neointimal thickening, scanning electron microscopic examination of the luminal surface, and histological evaluation of the tissue reaction to the implanted material.

2. Results

All devices were implanted successfully and the animals tolerated the procedures without complications. No test article related events occurred during the implant phase and all animals remained healthy with no signs of device related complications. Exposure of the adventitial surface of native vessel in the area of test article deployment indicated there was no adventitial inflammatory reaction to the test articles. Following bisection of the test articles, the luminal surface was evaluated grossly and no evidence of gross neointimal thickening or thrombus formation was observed. The test articles were subjected to scanning electron microscopic evaluation of the luminal surface which revealed complete endothelialization of the luminal surface of all devices. Histological evaluation revealed complete incorporation of the test articles into the native vessel wall. The neointimal lining was complete on all test articles and this endothelialization response resulted in a cell lining that exhibited anti-thrombogenic characteristics. There was no observation of mal-apposition of the devices and post-implant angiograms revealed no abnormalities in flow entering, passing through, or leaving the devices.

3. Conclusion

The results of this study at both time-points (28 and 90 days) support the safety of the iCast device when implanted into iliac vessels.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a prospective, multi-center, single-arm clinical study in the United States and in Germany under G060243 to establish a reasonable assurance of safety and effectiveness of iliac artery stenting using the iCast Covered Stent System for treatment of subjects with de novo or restenotic atherosclerotic disease of the iliac arteries. The data from the clinical study related to the iCast Covered Stent System were the basis for a PMA approval decision. A summary of the clinical study is presented below.

A. iCARUS Study Design

Patients were treated between October 18, 2007 to October 27, 2010. The database for this PMA reflected all data collected through October 31, 2013 and included 165 subjects enrolled in the trial from at 25 investigational sites. The iCARUS (iCast Atrium Registry Ultrasound Study) study was a prospective, multicenter, non-randomized, single-arm study performed to evaluate the safety and effectiveness of the iCast Covered Stent System in the treatment of patients with symptomatic claudication or rest pain and angiographic confirmation of de novo or restenotic lesions in the common and/or external iliac artery. The iCARUS Clinical Study Report described the baseline, procedure and follow-up data at 30 days, 6 months, 9 months (primary endpoint), 12 months, 24 months and 36 months post-procedure.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the iCARUS study was limited to patients who met the following inclusion criteria:

Inclusion Criteria

1. Subject was 18 years of age or older.
2. Subject had lifestyle limiting claudication or rest pain (Rutherford-Becker scale 2-4).

3. Presence of de novo and/or restenotic lesions in the common and/or external iliac artery.
4. Subject had single, bilateral or multiple target lesions that was/were ≥ 50% stenosed by visual estimate.
5. The target lesion(s) could be successfully crossed with a guide wire and dilated.
6. The target segment of subject's lesion(s) was between 5 and 12mm in diameter and less than 110mm in length.
7. Subject had angiographic evidence of a patent profunda or superficial femoral artery in the target limb.
8. Subject had provided written informed consent.
9. Subject was able and willing to adhere to the required follow-up visits and testing through month 36.
10. Subject was able and willing to adhere to the required follow-up medication regimen.

Patients were not permitted to enroll in the iCARUS study if they met any of the following exclusion criteria:

Exclusion Criteria

1. Presence of other non-target ipsilateral arterial lesions requiring treatment. Ipsilateral superficial femoral artery (SFA) lesions was allowed at the time of procedure after the target lesion had been treated successfully ≤ 30% residual stenosis, no embolization, no complications) and under the following circumstances:

   Criteria for SFA Intervention:

   a) Greater than 70% stenosis or occlusion of the SFA
   b) Stenosis of <15cm or occlusion of <5cm in length
   c) Adequate distal run-off (at least one patent infrapopliteal run-off vessel with < 50% stenosis)
   d) No high-risk lesion characteristics: thrombus containing lesion or excessive (dense fluoroscopic) calcification.

   In the case that the target lesion treatment was not successful, treatment of other lesions were to be planned at least 30 days post procedure.

   NOTE: Treatment of lesions in the contralateral limb was allowed during the index procedure, at the discretion of the investigator. Treatment of lesions in any other vascular bed (i.e., renal, coronary) was to be completed at least 30 days prior to enrollment in the study.

   In the case of Ipsilateral SFA treatment needed:

   If the subject required ipsilateral SFA treatment during the index procedure, an FDA indicated PTA or atherectomy device was allowed. If treatment was unsuccessful, (resulting in a flow limiting dissection, >50% residual stenosis or limb threatening ischemia) the investigator was then to implement his/her own institution's standard method of bailout for such conditions.

2. The target lesion(s) had adjacent, acute thrombus.
3. The target lesion(s) was highly calcified or was previously treated with a stent.

NOTE: It was acceptable to treat a target lesion in a vessel that had been treated with a stent during a previous procedure (minimum 6 months). The previously placed stent had to be patent (<15mm peak gradient and < 50% residual stenosis) and ≥ 2cm away from the target lesion in order to successfully attempt to treat the target lesion with the iCast Covered Stent and avoid overlapping of the stents. Intervention upon the previously placed stent was prohibited.

4. Target lesion involved the internal iliac artery resulting in crossing of the side-branch with the iCast Covered Stent (e.g., "jailing" of the side-branch).

   NOTE: If the internal iliac artery was totally occluded and not amenable to percutaneous recanalization, the operator was allowed to deploy an iCast Covered Stent across the orifice of the internal iliac artery if necessary to completely cover the target lesion.

5. Subject had an abdominal aortic aneurysm contiguous with the iliac artery target lesion.
6. Subject had a pre-existing target iliac artery aneurysm or perforation or dissection of the target iliac artery prior to initiation of the iCast implant procedure.
7. Subject had a post-surgical stenosis and anastomotic suture treatments of the target vessel.
8. Subject had a vascular graft previously implanted in the native iliac vessel.
9. Subject had tissue loss, defined as Rutherford-Becker classification category 5 or 6.
10. Subject had contrast agent hypersensitivity that could not be adequately pre-medicated, had a hypersensitivity to stainless steel, Eptfe or had intolerance to antiplatelet, anticoagulant, or thrombolytic medications.
11. History of neutropenia (WBC <3,000/mm^3), coagulopathy, or thrombocytopenia (platelet count <80,000/ Ml) that had not resolved or required treatment within 6-months of the index procedure.
12. Known bleeding or hypercoagulability disorder or significant anemia (Hb< 8.0 g/Dl) that could not be corrected.
13. Subject had one or more of the following laboratory values:
    a) Platelet count less than 80,000/ Ml,
    b) Prothrombin Time (PT)/partial thromboplastin time (PTT) not within normal limits (as determined by individual center)
    c) Serum creatinine level greater than 2.5 mg/Dl
14. Subject required general anesthesia for the procedure.
15. Subject was pregnant.
16. Subject had a co-morbid illness that could have resulted in a life expectancy of less than 1 year.
17. Subject was participating in an investigational study of a new drug, biologic or device at the time of study screening. NOTE: Subjects who were participating in the long term follow-up phase of a previously investigational and currently FDA-approved product were not excluded by this criterion.

2. Follow-up Schedule

After hospital discharge, patients were required to return to the study center for clinical assessments on Day 30 (± 7 days), 6-months (± 14 days), 9-months (± 14 days), 12-months (± 30 days), and annually thereafter through 36 months (± 30 days). Assessments including, but not limited to ECG (30 day only), Rutherford Becker score, ankle-brachial index (ABI), health status assessment, and duplex scans were performed. Additionally, an angiogram

was performed as needed to confirm restenosis and assess the safety and effectiveness of the iCast Covered Stent.

3. Clinical Endpoints

Primary Composite Endpoint

The primary endpoint of the iCARUS study was a composite endpoint defined as the occurrence of death within 30 days, target site revascularization (TSR) within 9 months, or restenosis at 9 months post-procedure (within the 240 - 312 day window of the 9-month visit). The determination of restenosis was made by direct evaluation of the iliac arteries using duplex ultrasound (or angiography done in lieu of ultrasound).

The expected 9-month composite endpoint rate was estimated based on published literature. The performance goal of 16.57% included the estimated endpoint rate of 9.67% plus a margin of 6.90%. The primary endpoint null and alternative hypotheses were:

$H_o: \pi_{iCast} \geq 16.57\%;$

$H_A: \pi_{iCast} < 16.57\%,$

where: π_{iCast} is the true primary endpoint rate for iCARUS.

The upper limit of the exact one-sided 95% confidence interval based on the observed composite endpoint rate at 9 months had to be lower than 16.57%. Meeting this condition (i.e., rejection of the null hypothesis: H_o) was the criterion to consider the study successful.

Using one-sided exact hypothesis testing based on the binomial distribution, the required total evaluable sample size for the one-sided significance testing was 150 (i.e., with a total evaluable sample size of 150, power is ≥80% to reject the above null-hypothesis in favor of the alternative, under the stated above assumptions). A total of 165 patients were enrolled to account for a 10% assumed loss to follow-up (LTFU).

Secondary Endpoints

The secondary endpoints were: Major Adverse Vascular Event (MAVE) at each timepoint through 12 months; Major Adverse Event (MAE) at 30 days; device success, acute procedural success, clinical success at each timepoint through 36 months; patency at each timepoint through 36 months; and a composite rate of 30-day death, 9-month TSR, and 9-month restenosis in subjects without total occlusions of the iliac artery with the following definitions:

- MAVE was defined as a composite rate of myocardial infarction at 30-days, stent thrombosis, clinically apparent distal embolization, defined as causing end-organ damage, arterial rupture, acute limb ischemia, target limb amputation or procedure related bleeding event requiring transfusion.
- MAE was defined as a composite rate of MAVE, any death, or stroke up to 30 days post-procedure.
- Device success was defined as the successful delivery and deployment of the study stent and intact retrieval of the delivery system.

- Acute procedural success was defined as device success with <30% residual stenosis immediately after stent placement, mean trans-stenotic pressure gradient <5 mmHg, and without occurrence of in-hospital MAVE.
- Early clinical success was defined as improvement of the Rutherford-Becker clinical criteria by ≥1 category, and assessed between baseline and the 1 month follow-up visit.
- Late clinical success was defined as a maintained improvement in ABI, assessed as either (1) Normalized (>0.90) or (2) An increase of 0.1 from the baseline level and not decreased by >0.15 from the maximum result (observed post-procedure). This endpoint was to be assessed during follow-up at the 6, 9, 12, 24, and 36 month visits.
- Patency was assessed at each follow-up time point, categorized as:
  - *Primary patency*, defined as continuous flow without revascularization, bypass, or target limb amputation.
  - *Primary assisted patency*, defined as continuous flow assisted when the target vessel has restenosed at any time post-procedure.
  - *Secondary patency*, defined as reestablishment of flow to distal arteries after occlusion has occurred at the target vessel.

For the components of the primary endpoint, the number and percentage of patients experiencing the outcome and the exact two-sided 95% confidence interval of the percentage was presented for the set of Intent to Treat (ITT) patients who had adequate follow up (i.e., all subjects who met the study entry criteria, signed the written informed consent, and were enrolled in the study). Results of each of the dichotomous secondary endpoints were evaluated descriptively.

B. iCARUS Accountability of PMA Cohort

At the time of database lock, of 165 patients enrolled in the PMA study, 76% (125) of patients were available for analysis at the completion of the study, the 36 month/ 3year post-operative visit. Between October 18, 2007 and October 27, 2010, a total of 165 subjects were enrolled at 25 investigational sites (24 US, 1 German site). Of the 165 subjects enrolled, 13 subjects had inclusion/exclusion violations. Ten of thirteen subjects did not meet one of the eligibility criteria. Three of the thirteen subjects did not meet multiple eligibility criteria. Protocol violations were reviewed by a Data Safety Monitoring Board (DSMB). The remaining 152 patients comprised the ITT Population.

Of the 152 subjects enrolled in the ITT Population, 152 subjects were eligible for the 30-day follow-up clinical visit and 140 subjects were eligible for the 9-month follow-up clinical visit. Twelve (12) subjects in the ITT population were not eligible for the 9-month follow up visit. Five (5) subjects died prior to the visit, two (2) subjects withdrew consent, and five (5) subjects were lost to follow-up. A total of 117 of 152 subjects were available for analysis at the 36 month/ 3 year post-operative visit. Thirteen (13) subjects died prior to the visit, seven (7) subjects withdrew consent, and fifteen (15) subjects were lost to follow-up.

Figure 2 provides a subject flow chart for the iCARUS study. Table 6 further details subject accountability through the 3-year Follow-up Visit for the ITT population.

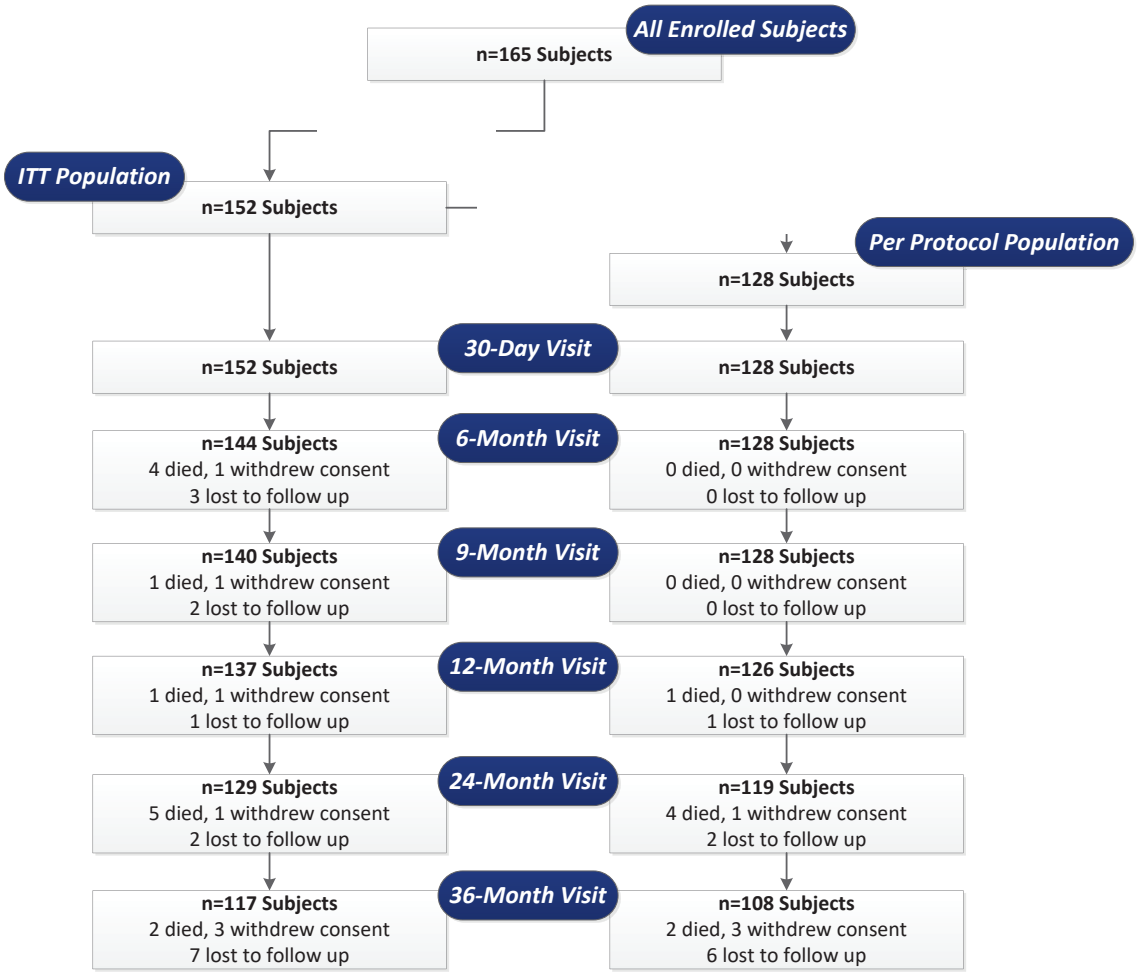

Figure 2: iCARUS Subject Flow Chart

Table 6: iCARUS Subject Follow-up Compliance - ITT Population

Subject Compliance	**N=152**
1-Month Follow-up	
Eligible Subjects[a]	152
Follow-up Compliance within Window[b] (%)	81.6 (124/152)
Follow-up within or outside of Window (%)	98.7 (150/152)
9-Month Follow-up	
Eligible Subjects[a]	140
Follow-up Compliance within Window[b] (%)	74.3 (104/140)
Follow-up within or outside of Window (%)	95 (133/140)
12-Month Follow-up	
Eligible Subjects[a]	137
Follow-up Compliance within Window[b] (%)	84.7 (116/137)
Follow-up within or outside of Window (%)	97.8 (134/137)
24-Month Follow-up	
Eligible Subjects[a]	129
Follow-up Compliance within Window[b] (%)	82.2 (106/129)
Follow-up within or outside of Window (%)	95.3 (123/129)

36-Month Follow-up	
Eligible Subjects[a]	117
Follow-up Compliance within Window[b] (%)	80.3 (94/117)
Follow-up within or outside of Window (%)	100 (117/117)

[a] Includes subjects that have not died, withdrawn consent and are not lost to follow up

[b] Within window visits are defined as: 1-month (23-37 days), 9-month (256-284 days), 12-month (330-390 days), 24-month (690-750 days), 36-month (1050-1110 days).

C. iCARUS Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for this type of study performed in the US. Table 7 presents baseline demographics and clinical characteristics. The iCARUS population was predominantly male (61.8%) with a history of smoking (91.4%), hypertension (84.9%) and hypercholesterolemia 85.5%). Table 8 and Table 9 summarize pre- and post-procedure lesion characteristics as assessed by the angiographic core laboratory. Two hundred twenty-three (223) lesions were treated in 206 limbs in 152 subjects. The majority of lesions had severe calcification (60.1%) pre-procedure. Among the 223 evaluable baseline lesions, mean reference vessel diameter (RVD) was 8.3±2.1mm, mean percent stenosis was 69.3±16.7% and mean minimum lumen diameter (MLD) was 2.6±1.5mm.

Table 7: iCARUS Subject Demographics, Medical History and Risk Factors - ITT Population

	N=152
Age	**Years**
Mean ± SD	65.2±10.0
Median	66.4
Range (Min, Max)	42.2,86.3
Sex	**% (m/n)**
Male	61.8 (94/152)
Female	38.2 (58/152)
Race	**% (m/n)**
American Indian or Alaska Native	0 (0/152)
Asian	0 (0/152)
Black or African American	5.3 (8/152)
Native Hawaiian or Other Pacific Islander	0 (0/152)
White	93.4 (142/152)
Other	1.3 (2/152)
Ethnicity	**% (m/n)**
Hispanic or Latino	2.0 (3/152)
Not Hispanic or Latino	98.0 (149/152)
Medical History and Risk Factors	**% (m/n)**
Previous Peripheral Artery Revascularization/surgery	16.7 (25/150)
Coronary Artery Disease	51.0 (77/151)
Previous Myocardial Infarction	23.2 (35/151)
Previous Percutaneous Coronary Revascularization	25.8 (39/151)
Coronary Artery Bypass Graft Surgery	22.5 (34/151)
Cerebrovascular Accident	7.2 (11/152)

Previous Amputation	1.3 (2/152)
Transient Ischemic Attack (TIA)	4.6 (7/151)
Diabetes Mellitus	36.8 (56/152)
Hypertension	84.9 (129/152)
Hypercholesterolemia	85.5 (130/152)
Renal Insufficiency	12.5 (19/152)
Cigarette Smoking Status	**% (m/n)**
Current Smoker	50.3 (76/151)
Former Smoker	41.1 (62/151)
Non-Smoker	8.6 (13/151)

m=number of subjects in the category
n=number of subjects in the study group with sufficient data for analysis

Table 8: iCARUS Angiographic Morphology Data - ITT Population (N=152)

Lesion Characteristics	**Lesions N= 223 %(m/n)**
Pre-Procedure Assessment	
Eccentric	49.3% (110/223)
Ulceration	28.7% (64/223)
Totally Occluded	12.1% (27/223)
Calcification	
None/Mild	12.6% (28/223)
Moderate	27.4% (61/223)
Severe	60.1% (134/223)
Thrombus	
None	99.6% (222/223)
Possible Thrombus	0.4% (1/223)
Post-Procedure Assessment Dissection Grade	
None	91.0% (202/222)
A	0.0% (0/222)
B	5.0% (11/222)
C	3.6% (8/222)
D	0.5% (1/222)
E	0.0% (0/222)
F	0.0% (0/222)

m= number of lesions in the category
n = number of lesions in the study group with sufficient data for analysis

Table 9: iCARUS Angiographic Quantitative Analysis - ITT Population

Lesion Characteristics	**N=152 Lesions = 223**			
	n	**Mean+/-SD**	**Median**	**Min-Max**
Lesion Length	**223**	**25.4 ± 16.8**	**20.4**	**0.0, 90.0**
Pre-Procedure Assessment				
Reference Vessel Diameter (mm)	223	8.3± 2.1	8.1	4.1, 16.7
Percent Stenosis (most severe) (%)	223	69.3 ± 16.7	66.2	26.7, 100.0

Lesion Characteristics	N=152 Lesions = 223			
	n	Mean+/-SD	Median	Min-Max
Lesion Length	**223**	**25.4 ± 16.8**	**20.4**	**0.0, 90.0**
Minimum Lumen Diameter (mm)	223	2.6 ± 1.5	2.7	0.0, 7.9
Post-Procedure Assessment (in stent)				
Reference Vessel Diameter (mm)	222	8.4± 2.1	8.1	4.1, 17.0
Percent Stenosis (most severe) (%)	222	11. 8 ± 9.9	12.4	-21.2, 40.8
Minimum Lumen Diameter (mm)	222	7.3±1. 7	7.1	3.7, 13.1

n = number of lesions in the study group with sufficient data for analysis

D. Primary Safety and Effectiveness Results

The primary endpoint was a composite endpoint of the occurrence of death within 30 days, TSR within 9 months, or restenosis detected by duplex ultrasound of the iliac artery (or angiography done in lieu of ultrasound) at 9-months post-procedure.

The Intent-to-Treat (ITT) population (n=152) was comprised of all subjects who met the study entry criteria, signed the written informed consent, and were enrolled in the study. The primary composite endpoint rate, based on available cases in the ITT population, was 8.1% 10/123), with an exact one-sided upper 95% confidence interval (CI) of 13.4% p=0.005). This was below the protocol-specified performance goal of 16.57% and the study stent was considered to have met the performance goal (Table 10).

Table 10: iCARUS Primary Composite Endpoint - ITT Population

Endpoint	ITT Population (N=152) %(m/n)	Exact one-sided upper 95% CI limit	Assessment of Primary Endpoint Rate < 16.57%
Primary Composite Endpoint to 9-Months (Available Cases)	**8.1% (10/123)**	**13.4%**	**p=0.005**
Death to 30 days	0.0% (0/151)		
TSR within 9-Months	2.9% (4/139)		
Restenosis at 9-Months	4.9% (6/123)		

m = number of lesions in the category
n = number of lesions in the study group with sufficient data for analysis

1. Safety Results

An independent Clinical Events Committee (CEC) adjudicated all cases of death, TSR and other MAVEs/MAEs. Restenosis was adjudicated by an independent core laboratory. Clinical sites also reported all Adverse Events that occurred. Serious Adverse Events (SAEs) that occurred throughout the study for all subjects enrolled are listed in Table 11. Results were similar in the ITT population.

A total of 44 of 165 (26.7%) enrolled subjects experienced SAEs to 9-months. The most frequent SAEs were in the vascular disorders MedDRA System Organ Class (SOC) (14/165) and the cardiac SOC (13/165). A total of 86 of 165 (52.1%) enrolled subjects experienced SAEs to 36-months. The most frequent SAEs were in the vascular disorders SOC (30/165) and the cardiac SOC (33/165).

There were 14 deaths total reported in the study (six (6) deaths reported prior to 9-months). None of the deaths were deemed to be related to the study procedure or the study device. There were no unanticipated adverse device effects (UADEs) reported in the study.

Table 11: iCARUS Summary of Serious Adverse Events (SAEs) - All Enrolled Subjects (N=165)

System Organ Class (SOC)/Preferred Term	Subjects with events to 9 months	Subjects with events to 36 months
Any SAE	44(26.7%)	86(52.1%)
Blood and Lymphatic System Disorders(Anaemia, Haemorrhagic anaemia)	2(1.2%)	3(1.8%)
Cardiac Disorders (Acute coronary syndrome[a], Acute myocardial infarction, Angina pectoris, Angina unstable, Atrial fibrillation, Atrial flutter[a], Atrioventricular block, Cardiac arrest[a], Cardiac failure, Cardiac failure congestive, Cardio-respiratory arrest, Coronary artery disease, Coronary artery occlusion[a], Myocardial infarction, Stress cardiomyopathy[a], Ventricular tachycardia)	13(7.9%)	33(20.0%)
Ear and Labyrinth Disorders (Vertigo[a])	0	1(0.6%)
Gastrointestinal Disorders (Abdominal pain[a], Colitis[a], Gastritis[a], Gastrointestinal haemorrhage, Intestinal obstruction[a], Intestinal perforation, Nausea[a], Pancreatitis[a], Pancreatitis acute[a], Peritonitis[a], Rectal haemorrhage[a], Small intestine obstruction[a], Upper gastrointestinal haemorrhage, Vomiting[a])	5(3.0%)	13(7.9%)
General Disorders and Administration Site Conditions (Asthenia, Catheter site haematoma, Chest pain, Impaired healing[a], Non-cardiac chest pain[a])	6(3.6%)	10(6.1%)
Hepatobiliary Disorders (Cholecystitis[a], Hepatic steatosis[a])	0	2(1.2%)
Immune System Disorders (Anaphylactic reaction)	1(0.6%)	2(1.2%)
Infections and Infestations (Abdominal abscess, Bronchitis[a], Bronchitis bacterial[a], Cellulitis[a], Gastroenteritis viral[a], Groin abscess[a], Influenza[a], Pneumonia, Pneumonia staphylococcal[a], Post procedural sepsis[a], Sepsis, Urosepsis[a])	6(3.6%)	18(10.9%)

System Organ Class (SOC)/Preferred Term	Subjects with events to 9 months	Subjects with events to 36 months
Injury, Poisoning, and Procedural Complications (Abdominal wound dehiscence[a], Anaemia postoperative[a], Aortic injury[a], Arterial injury, Device dislocation[a], Femur fracture, In-stent arterial restenosis, Incisional hernia[a], Postoperative ileus[a], Spinal fracture[a], Stent occlusion[a], Subdural haematoma, Tendon injury[a], Traumatic brain injury[a], Urostomy complication[a], Vascular graft occlusion[a])	5(3.0%)	19(11.5%)
Metabolism and Nutrition Disorders (Acidosis[a], Fluid overload[a], Hyperkalaemia[a], Hypoglycaemia, Hyponatraemia, Obesity[a])	2(1.2%)	6(3.6%)
Musculoskeletal and Connective Tissue Disorders (Arthralgia[a], Arthritis, Fistula[a], Muscular weakness[a], Osteoarthritis, Rhabdomyolysis[a])	2(1.2%)	7(4.2%)
Neoplasm Benign, Malignant, and Unspecified (cysts and polyps) (Bronchial carcinoma[a], Colon cancer, Colon cancer recurrent[a], Hepatic neoplasm malignant[a], Lung cancer metastatic, Lung neoplasm malignant, Lymphoma[a], Metastases to liver, Prostate cancer[a], Transitional cell carcinoma[a])	3(1.8%)	9(5.5%)
Nervous System Disorders (Brain mass[a], Carotid artery stenosis, Cerebrovascular accident, Encephalopathy, Polyneuropathy[a], Subarachnoid haemorrhage, Syncope, Syncope vasovagal[a], Transient ischaemic attack)	7(4.2%)	14(8.5%)
Psychiatric Disorders (Depression)	1(0.6%)	1(0.6%)
Renal and Urinary Disorders (Calculus ureteric[a], Renal artery occlusion[a], Renal artery stenosis[a], Renal disorder[a], Renal failure[a], Renal failure acute, Renal failure chronic, Renal mass[a])	2(1.2%)	13(7.9%)
Reproductive System and Breast Disorders (Galactorrhoea[a])	0	1(0.6%)
Respiratory, Thoracic, and Mediastinal (Acute respiratory failure[a], Chronic obstructive pulmonary disease[a], Dyspnoea[a], Epistaxis, Pleural effusion[a], Pneumonia aspiration, Pneumothorax[a], Pulmonary embolism[a], Pulmonary mass[a], Pulmonary oedema, Respiratory failure[a])	2(1.2%)	10(6.1%)
Skin and Subcutaneous Tissue Disorders (Psoriasis[a], Skin ulcer[a])	0	2(1.2%)
Vascular Disorders (Aortic stenosis[a], Arterial restenosis, Arterial thrombosis limb, Femoral	14(8.5%)	30(18.2%)

System Organ Class (SOC)/Preferred Term	Subjects with events to 9 months	Subjects with events to 36 months
arterial stenosis, Femoral artery occlusion, Haemorrhage[a], Hypotension, Iliac artery stenosis, Intermittent claudication, Orthostatic hypotension, Peripheral arterial occlusive disease, Peripheral artery aneurysm[a], Peripheral ischaemia[a], Peripheral vascular disorder[a], Subclavian artery stenosis, Vascular pseudoaneurysm)		

[a] Preferred Term applies to events to 36 months only
m= number of lesions in the category
n = number of lesions in the study group with sufficient data for analysis

2. Secondary Safety and Effectiveness Endpoint Results

Secondary endpoints included MAVE and MAE as adjudicated by the independent CEC, device success, acute procedural success (with and without pressure gradient), clinical success, patency (primary, primary-assisted, and secondary), and a composite rate consisting of 30-day death, 9-month TSR, and 9-month restenosis in subjects without iliac total occlusions.

MAVEs are summarized through 12-months post-procedure (Table 12). In the ITT population, 4.6% (7/151) of subjects experienced at least one MAVE to 30 days and 6.9% (10/144) of subjects experienced at least one MAVE to 6 months. The most common MAVE event was procedure-related bleeding event that required transfusion. This type of event occurred among 4 of 151 (2.6%) ITT subjects to 30 days, and among 7 of 144 (4.9%) subjects to 6 months. There were no additional subjects experiencing MAVE events beyond 6-months post-procedure, for a total MAVE rate of 7.1% (10/140) at 9 months and 7.2% (10/139) at 1 year.

Eight of 151 (5.3%) subjects experienced a MAE to 30 days 7 subjects experienced a MAVE and 1 subject experienced a stroke). There were no deaths in the ITT population reported to 30 days.

Acute procedural success was achieved in 92.7% (140/151) of subjects. In the eleven subjects that did not achieve acute procedural success, seven subjects experienced an in-hospital MAVE; three subjects had residual stenosis >30%; and two subjects were documented as device non-success. Note that the eleven subjects includes one subject that experienced both device non-success as well as residual stenosis >30%. One additional subject was missing angiography and was not assessed for acute procedural success, though the subject achieved device success and had no in-hospital MAVE.

Primary patency was achieved in 100.0% of the ITT subjects at 1-month, 99.3% of the subjects at 6-months and 96.4% of the subjects at 9-months. Primary patency was 93.5% at 12 months, 87.6% at 24 months and 84.7% at 36 months. Primary-assisted patency was achieved in all (100.0%) of subjects at 1, 6, 9 and 12 months, in 99.2% of subjects at 24 months, and 99.1% of subjects at 36 months. Secondary patency was achieved in all

(100.0%) subjects at all time points through 36 months post-procedure. Device, procedural and clinical success results are listed in Table 12.

Table 12: iCARUS Secondary Endpoints - ITT Population
Subjects = 152, Lesions = 223, Limbs = 206

Endpoint	ITT Population (N=152) % (m/n)	95% CI
Major Adverse Vascular Events (MAVE)		
MAVE to 30-Days	4.6% (7/151)	[1.9%, 9.3%]
MAVE to 6 months	6.9% (10/144)	[3.4%, 12.4%]
MAVE to 9 months	7.1% (10/140)	[3.5%, 12.7%]
MAVE to 12 months	7.2% (10/139)	[3.5%, 12.8%]
Major Adverse Events (MAE)	5.3% (8/151)	[2.3%, 10.2%]
Device Success	98.7% (150/152)	[95.3%, 99.8%]
Acute Procedural Success	78.2% (111/142)	[70.5%, 84.7%]
Acute Procedural Success (without Pressure Gradient)	92.7% (140/151)	[87.3%, 96.3%]
Clinical Success		
Early Clinical Success	88.7% (133/150)	[82.5%, 93.3%]
Late Clinical Success by 6-Months	63.5% (80/126)	[54.4%, 71.9%]
Late Clinical Success by 9-Months	76.6% (98/128)	[68.3%, 83.6%]
Late Clinical Success by 12-Months	67.2% (86/128)	[58.3%, 75.2%]
Late Clinical Success by 24-Months	70.8% (80/113)	[61.5%, 79.0%]
Late Clinical Success by 36-Months	72.4% (76/105)	[62.8%, 80.7%]
Patency at 1-Month		
Primary	100.0% (151/151)	[97.6%, 100.0%]
Primary Assisted Patency	100.0% (151/151)	[97.6%, 100.0%]
Secondary Patency	100.0% (151/151)	[97.6%, 100.0%]
Patency at 6-Months		
Primary	99.3% (143/144)	[96.2%, 100.0%]
Primary Assisted Patency	100.0% (144/144)	[97.5%, 100.0%]
Secondary Patency	100.0% (144/144)	[97.5%, 100.0%]
Patency at 9-Months		
Primary	96.4% (134/139)	[91.8%, 98.8%]
Primary Assisted Patency	100.0% (139/139)	[97.4%, 100.0%]
Secondary Patency	100.0% (139/139)	[97.4%, 100.0%]
Patency at 12-Months		
Primary	93.5% (129/138)	[88.0%, 97.0%]
Primary Assisted Patency	100.0% (138/138)	[97.4%, 100.0%]
Secondary Patency	100.0% (138/138)	[97.4%, 100.0%]
Patency at 24-Months		
Primary	87.6% (113/129)	[80.6%, 92.7%]
Primary Assisted Patency	99.2% (128/129)	[95.8%, 100.0%]
Secondary Patency	100.0% (129/129)	[97.2%, 100.0%]
Patency at 36-Months		
Primary	84.7% (100/118)	[77.0%, 90.7%]
Primary Assisted Patency	99.1% (114/115)	[95.3%, 100.0%]

Endpoint	ITT Population (N=152) % (m/n)	95% CI
Secondary Patency	100.0% (115/115)	[96.8%, 100.0%]

m= number of lesions in the category
n = number of lesions in the study group with sufficient data for analysis

3. iCARUS Subgroup Analysis

The following preoperative characteristics were evaluated for potential association with outcomes:

- Subjects with/without total occlusions and
- Gender.

As dictated by the protocol and the nature of the iCARUS study design, the pre-specified subgroup analyses performed did not include formal statistical comparisons between the different groups analyzed.

Study Results for Subjects With/Without Total Occlusions

The overall primary composite endpoint rate, based on available cases in the ITT population, is 8.1% (10/123). Table 13 shows the primary composite endpoint rates for subgroups of subjects with and without total occlusions; which was 21.7% (5/23) and 5% (5/100), respectively.

There is an overlap of the 95% confidence intervals of the primary composite endpoint rates for the subjects with and without total occlusions ([7.5%, 43.7%] and [1.6%, 11.3%], respectively). Given the low number of subjects with total occlusions, and the limitations of the study design itself, this indicates that there is no strong evidence to suggest that the primary composite endpoint rates between groups are different.

Table 13: iCARUS Primary Endpoint to 9-Months for Subjects without Total Occlusion – ITT Population

ITT Population (N=126)	Total Occlusion (N=26) %(m/n)	Non-total Occlusion (N=126) %(m/n)
Primary Composite Endpoint	21.7% (5/23)	5.0% (5/100)
Death to 30 days	0.0% (0/26)	0.0% (0/125)
TSR within 9-Months	8.3% (2/24)	1.7% (2/115)
Restenosis at 9-Months	13.0% (3/23)	3.0% (3/100)

m= number of subjects in the category
n = number of subjects in the study group with sufficient data for analysis

Study Results by Gender

The overall primary composite endpoint rate, based on available cases in the ITT population, is 8.1% (10/123). Table 14 shows the primary composite endpoint rates for gender subgroups; which was 6.3% (5/79) for males and 11.4% (5/44) for females.

There is an overlap of the 95% confidence intervals of the primary composite endpoint rates for the male and female populations ([2.1%, 14.2%] and [3.8%, 24.6%], respectively) with a Fisher's exact p-value of 0.33, which indicates that there is no strong evidence to suggest that the rates between male and female populations are different. Therefore, there is not enough evidence to assess that the percentage difference in primary composite endpoint rates (6.3% vs. 11.4%) is significant or by chance.

The overall 30-day MAVE and MAE rates are 4.6% and 5.3%, respectively. Table 14 shows the secondary 30-day endpoints for gender subgroups. Thirty-day MAVE rates were 2.1% (2/94) for males and 8.8% (5/57) for females. There is an overlap of the 95% confidence intervals of the MAVE rates for the male and female populations ([0.3%, 7.5%] and [2.9%, 19.3%], respectively), with a Fisher's exact p-value of 0.1045, which indicates that there is no strong evidence to suggest that the rates between male and female populations are different. Similarly, thirty-day MAE rates were 3.2% (3/94) for males and 8.8% (5/57) for females. There is an overlap of the 95% confidence intervals of the MAE rates for the male and female populations ([0.7%, 9.0%] and [2.9%, 19.3%], respectively), with a Fisher's exact p-value of 0.1545, which indicates that there is no strong evidence to suggest that the rates between male and female populations are different.

Table 14: iCARUS Primary Endpoint to 9-Months by Gender – ITT Population

ITT Population (N=152)	**Males (N=94) %(m/n)**	**Females (N=58) %(m/n)**
Primary Composite Endpoint	6.3% (5/79)	11.4% (5/44)
Death to 30 days	0.0% (0/94)	0.0% (0/57)
TSR within 9-Months	2.3% (2/88)	3 .9% (2/51)
Restenosis at 9-Months	3.8% (3/79)	6.8% (3/44)

m= number of subjects in the category
n = number of subjects in the study group with sufficient data for analysis

Table 15: iCARUS Secondary Endpoints to 30 Days by Gender – ITT Population

ITT Population (N=152)	**Males (N=94) %(m/n)**	**Females (N=58) %(m/n)**
Major Adverse Vascular Events to 30 days	2.1% (2/94)	8.8% (5/57)
Myocardial Infarction at 30 days	1.1% (1/94)	1.8% (1/57)
Stent Thrombosis	0.0% (0/94)	0.0% (0/57)
Clinically apparent distal embolization	0.0% (0/94)	1.8% (1/57)
Arterial rupture	1.1% (1/94)	0.0% (0/57)
Acute Limb Ischemia	0.0% (0/94)	3.5% (2/57)
Target Limb Amputation	0.0% (0/94)	0.0% (0/57)
Procedure related bleeding event requiring transfusion	0.0% (0/94)	7.0% (4/57)
Major Adverse Event (MAE)	3.2% (3/94)	8.8% (5/57)
MAVE to 30 days	2.1% (2/94)	8.8% (5/57)
Death to 30 days	0.0% (0/94)	0.0% (0/57)

ITT Population (N=152)	Males (N=94) %(m/n)	Females (N=58) %(m/n)
Stroke to 30 days	1.1% (1/94)	0.0% (0/57)

m= number of subjects in the category
n = number of subjects in the study group with sufficient data for analysis

4. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population. Peripheral artery disease is not typically found in pediatric populations with the exception of rare homozygous lipid disorders. Accordingly, the safety and effectiveness of the iCast Covered Stent System in pediatric populations were not studied in the iCARUS trial.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 152 investigators of which none were full-time or part-time employees of the sponsor and four (4) had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: None
- Significant payment of other sorts: Four
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: None

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. COBEST Study Design

The Covered Versus Balloon Expandable Stent Trial (COBEST) was an Investigator-initiated prospective, multi-center, randomized controlled trial performed to determine if covered stents offer a patency advantage over bare metal stents in the treatment of aortoiliac arterial

occlusive disease. The first publication by Mwipatayi et al.[1] described the baseline, procedure and follow up data at 1, 6, 12 and 18 months for 125 subjects (168 individual iliac arteries) enrolled in the trial from January 2006 through December 2008. In this study, 83 vessels received an Advanta V12 covered stent (note: iCast Covered Stent is marketed outside the U.S. under the name of Advanta V12 Covered Stent) and 85 vessels received a balloon expandable or self-expandable bare metal stent, which varied but included Palmaz Genesis and Smart (Cordis Corp, East Bridgewater, NJ), Express LD iliac stent (Boston Scientific, Natick, MA), Assurant Cobalt iliac stent and AVE-Bridge (Medtronic, Minneapolis, MN), Peiron (Biotronik, Berlin, Germany) and Edwards Life Stent (Bard Peripheral Vascular Inc., Tempe, AZ).

A subsequent publication by Mwipatayi et al.[2] described post-hoc analysis of primary, primary-assisted and secondary patency rates through 5 years for 77 subjects (119 iliac arteries).

Primary Endpoint

The primary endpoint of the COBEST study was the rate of binary restenosis, defined by ≥ 50% reduction in lumen diameter and freedom from stent occlusion at 18 months. These were determined by duplex ultrasound imaging, computed tomography angiography (CTA), or catheter biplane digital subtraction angiography (DSA). Subjects were assessed clinically with ABI and aortoiliac artery duplex at 1, 6, 12 and 18 months. If the duplex scan was inconclusive, a CTA or DSA or both were performed to determine if the primary endpoint had been achieved.

Secondary Endpoints

Secondary endpoints were determined anatomically, clinically and hemodynamically. Anatomic endpoints included stent patency, stent integrity and target vessel revascularization (TVR), defined as any repeat percutaneous intervention or surgical bypass of the segment of the target vessel. The target vessel was defined as the entire aortoiliac vessel proximal and distal to the target lesion. TVR was typically driven by clinical evidence of symptoms or positive stress-induced significant symptoms (treadmill exercise ABI).

The clinical endpoints were major amputation above the ankle and major adverse events resulting in subject hospitalization or prolongation of existing hospitalization, significant physical disability, or death. The hemodynamic endpoint was a change in ABI between baseline and measurements at 1, 6, 12, and 18 months.

Long Term Patency and Survival

As part of the post hoc analysis through 5 years, the rate of primary patency, defined as uninterrupted patency (absence of stenosis of >50% or occlusion of the treated segment

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[1] Mwipatayi, B.P., et al., *A comparison of covered vs bare expandable stents for the treatment of aortoiliac occlusive disease.* J Vasc Surg, 2011. **54**(6): p. 1561-70.

[2] Mwipatayi, B.P., et al., *Durability of the balloon-expandable covered versus bare-metal stents in the Covered versus Balloon Expandable Stent Trial (COBEST) for the treatment of aortoiliac occlusive disease.* J Vasc Surg, 2016. **64**(1): p. 83-94 e1.

determined by imaging) with no procedures performed on or at the margins of the treated segment, was collated through 5 years to evaluate durability of results originally obtained through 18 months. Assisted primary patency (a stent re-stenosis of >50% requiring intervention), secondary patency (an occluded stent requiring intervention) and freedom from all cause death were also evaluated through 5 years.

B. COBEST Safety and Effectiveness Results

Primary Endpoint Results

The primary endpoint was the rate of binary restenosis and freedom from stent occlusion at 18 months. Aortoiliac lesions treated with an Advanta V12 (iCast) covered stent were significantly more likely to remain free from binary restenosis at 18 months than those that were treated with a bare metal stent (Hazard Ratio (HR), 0.354; 95% CI, 0.153-0.819; p=0.0243) (see Figure 3). Binary restenosis was documented in 8 arteries in the Advanta V12 (iCast) group and in 20 in the bare metal stent group.

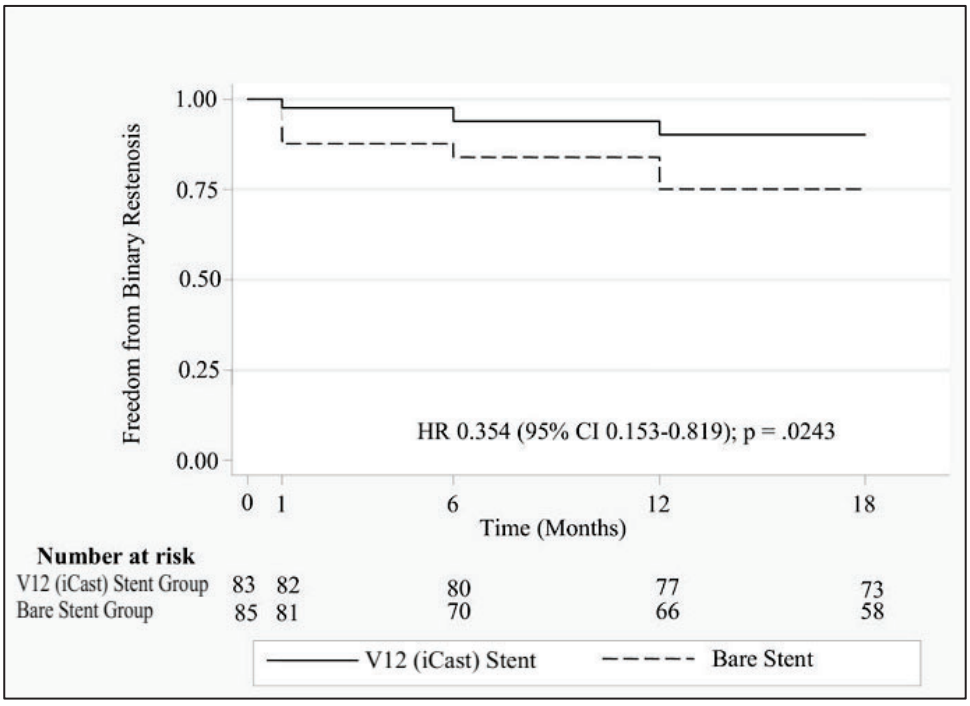


Figure 3: COBEST Freedom from Binary Restenosis

Kaplan-Meier curves for Freedom from binary restenosis for the ITT population. *CI*, Confidence interval; *HR*, hazard ratio. Note: the iCast Covered Stent is marketed outside the U.S. under the name of Advanta V12 Covered Stent.

This significant difference in freedom-from binary restenosis was noted for TASC C and D lesions (HR, 0.136; 95% CI, 0.042-0.442; p=0.0056); however, no significant difference was noted for TASC B lesions (HR, 0.748; 95% CI, 0.235-2.386, p=0.6229).

Complete occlusions of the stented lesion during the follow-up period occurred in three (3) patients in the covered-stent group and in ten (10) patients in the bare metal stent group; however, this difference was not statistically significant (HR, 0.279; 95% CI, 0.072-1.083; p=0.0874).

Secondary Endpoint Results

TVR during the study period demonstrated that there was less reintervention in the covered-stent group compared with the bare metal stent group (OR, 0.21; 95% CI, 0.07-0.64; p=0.006). Most of the reinterventions were performed at 12 and 18 months (Figure 4). Three patients from the bare metal stent group underwent aortobifemoral bypass grafting.

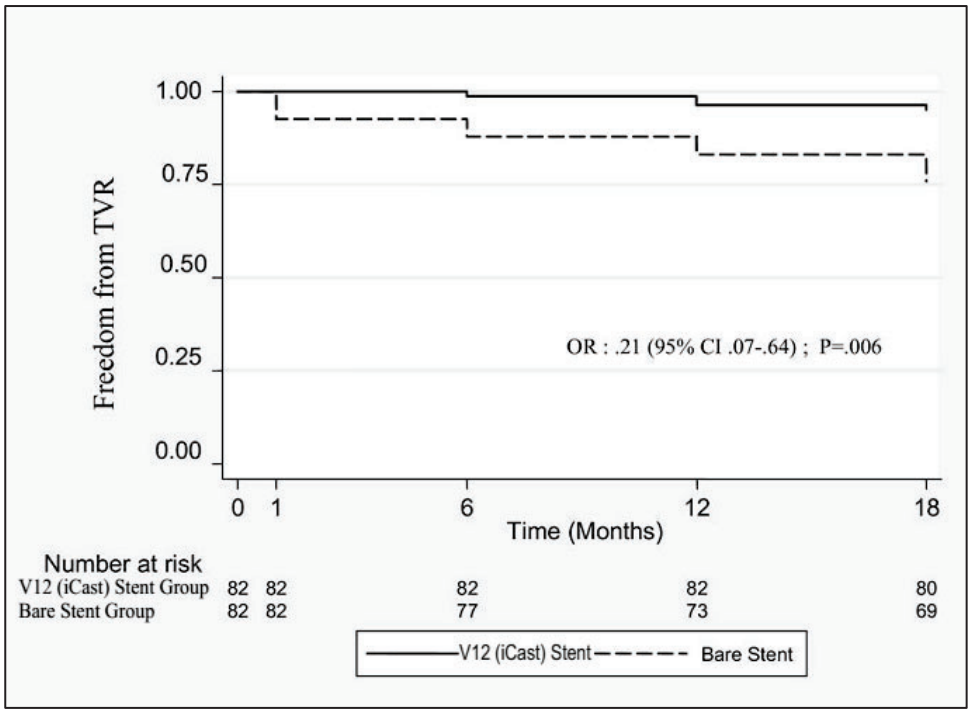


Figure 4: COBEST Freedom from Target Vessel Revascularization

Kaplan-Meier curves for Freedom from target vessel revascularization during the study period. *CI*, Confidence interval; *OR*, odds ratio; *TVR*, target vessel revascularization. Note: the iCast Covered Stent is marketed outside the U.S. under the name of Advanta V12 Covered Stent.

Four amputations were performed during the study period. Two patients with Advanta V12 (iCast) covered stents had below knee amputation at 18 months, which was likely related to uncontrollable diabetes mellitus and progression of infragenicular arterial disease. Two patients with bare metal stents had above knee amputations at 18 months due to a combination of factors. The difference between the two groups was not statistically significant (Odds Ratio 1.02; 95% CI 0.089-11.73; p=0.984).

ABI measurements during the follow-up period were not significantly different between the two groups at 1 and 6 months. However, the difference became statistically significant at 12 months (p=0.014) and had marginal significance at 18 months (p=0.07), suggesting long-term improvement in ABIs in the covered-stent group. For values, see Table 16.

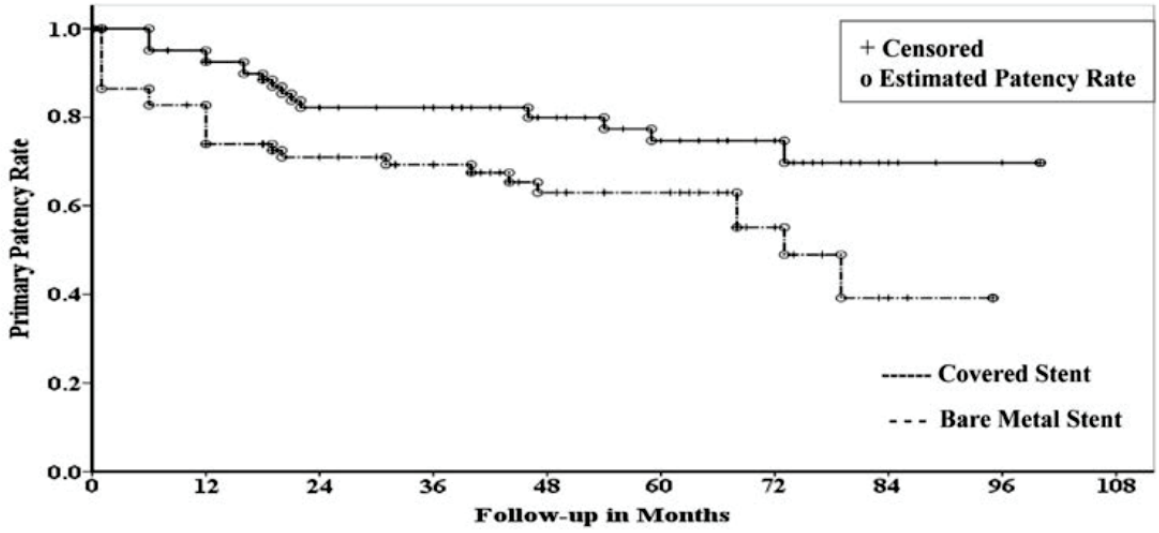
Table 16: Resting Ankle-Brachial Index on Side of the Lesion

Resting ABI	V12 Stent		Bare Stent		P
	No	Mean ± SEM	No	Mean ± SEM	
Baseline	75	0.65 ± 0.03	78	0.63 ± 0.03	0.639
1 month	71	0.91 ± 0.03	72	0.91 ± 0.03	0.927
6 months	73	0.89 ± 0.02	74	0.88 ± 0.03	0.653
12 months	75	0.94 ± 0.02	79	0.85 ± 0.03	0.014
18 months	70	0.94 ± 0.02	73	0.86 ± 0.03	0.07
SEM, Standard error of the mean					

Long Term Patency and Survival Results

The primary patency rates for the Advanta V12 (iCast) group at 18, 24, 48 and 60 months were 88.5%, 82.2%, 79.9% and 74.7%, respectively; the corresponding rates for the bare metal stent group were 73.9%, 70.9%, 63%, and 62.9% respectively (HR, 6.59; log-rank test, p=0.01) as shown in Figure 5.

The Kaplan-Meier survival estimates showed no significant difference between stent types for TASC B lesions (HR, 1.663; 95% CI, 61.657-75.545; p=0.197). Conversely, there was a statistically significant benefit when the Advanta V12 (iCast) covered stents were used in TASC C and D lesions compared with a bare metal stent (HR, 3.302; 95% CI, 54.253-75.753; p=0.003).



Time (Months)	0	12	24	36	48	60	72	84	96
Advanta V12 Stent (n. at risk)	83	74	52	47	35	28	17	5	2
Standard Error (%)	-	2.95	4.54	4.54	4.93	5.84	5.84	7.27	7.27
BMS (n. at risk)	85	66	46	40	28	23	10	3	1
Standard Error (%)	-	4.89	5.13	5.27	5.94	5.94	7.36	11.2	11.2

Figure 5: COBEST Kaplan-Meier Curve of Overall Primary Patency Rates of Both Stent Groups

The assisted primary patency rates for the Advanta V12 (iCast) covered stent group at 18, 24, 48 and 60 months were 96.1%, 89.7%, 86.8% and 83.7%, respectively; the corresponding rates for the bare metal stent group were 86.3%, 83.6%, 77.9%, and 76.1 % respectively (HR, 5.66; log-rank test, p=0.017).

The overall secondary patency was 96.3% in the Advanta V12 (iCast) covered stent group versus 87.3% in the bare metal stent group at 60 months follow up (log-rank test, p=0.033).

During the 5-year analysis period, the all-cause mortality rate was 19.5% in the covered stent group and 23.5% in the bare metal stent group (p=0.524).

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRE-CLINICAL AND CLINICAL STUDIES

A. Safety and Effectiveness Conclusions

Comprehensive preclinical bench, *in vitro* and *in vivo* testing was performed on the iCast Covered Stent System in accordance with national and international standards and guidances. Non-clinical testing included biocompatibility, *in vitro* bench, sterility and animal studies. The testing demonstrated that the iCast Covered Stent System met its performance and design specifications throughout its 3-year shelf life. A prospective multi-center, single-arm clinical trial (iCARUS) demonstrated that the iCast Covered Stent System is safe and effective for its intended use as a treatment for iliac artery disease in the indicated population. This clinical trial compared the safety and effectiveness of the iCast Covered Stent System to a predetermined performance metric. The composite safety and effectiveness endpoint was defined as the occurrence of death within 30 days, target site revascularization (TSR) within 9 months, or restenosis at 9 months post-procedure (as determined by DUS). The primary composite endpoint rate was 8.1% 10/123), with an exact one-sided upper 95% CI of 13.4% (p=0.005) and met the performance goal of 16.57% (p=0.005).

There were no deaths within 30 days, the rate of TSR within 9-months was 2.9%, and the restenosis rate at 9-months was 4.9%. Although no formal performance metric was designated for other secondary safety and effectiveness endpoints, analysis of key pre-specified endpoints is consistent with a low rate of MAVE, and MAE, and a high rate of early and late clinical and angiographic success with use of the iCast stent.

The benefits of stenting with the iCast Covered Stent System were maintained in the majority of subjects during long-term follow-up. At 36 months, primary patency was present in 84.7% of subjects, primary-assisted patency was present in 99.1%, and 100% of subjects in the ITT population had secondary patency. Similarly, late clinical success was present in 72.4% of subjects at this time point. These data are consistent with comparable long-term effectiveness data available for other approved iliac stents and support the safety and effectiveness of the iCast Covered Stent System when used for revascularization of iliac artery lesions. These results were consistent with supplementary clinical results from the COBEST study. Altogether, these data support the safety and effectiveness of the iCast Covered Stent System when used for revascularization of iliac lesions in the studied patient population.

B. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The primary potential benefit of the iCast Covered Stent System is the improvement or restoration of blood flow in the iliac arteries. In this study, the benefits of stenting with the iCast Covered Stent were maintained in the majority of subjects during long-term follow-up at 36 months. Clinical success and primary patency assessments did not show significant unexpected degradation in performance comparing 9 months to 36 months. Overall, the clinical data obtained are consistent with comparable long-term effectiveness data available for other approved iliac stents and support the safety and effectiveness of the iCast Covered Stent System when used for revascularization of iliac artery lesions. The risks associated with balloon-expandable stents are well-understood, and the frequency and types of adverse events reported throughout the pivotal clinical study are in alignment with expectations for the studied patient

population and therapeutic area. No unanticipated device- or procedure-related adverse events were reported in the study.

Given the available information from the non-clinical, pre-clinical, and clinical studies, the data support that the probable benefits outweigh the probable risks for using the iCast Covered Stent System for improving luminal diameter in patients with symptomatic atherosclerotic disease of the native common and/or external iliac arteries up to 110 mm in length, with a reference vessel diameter of 5 to 10 mm.

1. Patient Perspectives

   This submission did not include specific information on patient perspectives for this device.

C. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The clinical study met the pre-specified composite safety and effectiveness endpoint. Therefore, it is reasonable to conclude that the benefits of use of the stent for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use (IFU).

XIV. CDRH DECISION

CDRH issued an approval order on March 22, 2023.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.