Instructions For Use

iCast
covered stent system

GETINGE

Instructions For Use

1.0 Description

The iCast® covered stent system is a balloon-expandable stent, made of 316L stainless steel and encapsulated with expanded PTFE (ePTFE). The delivery system comprises an over-the-wire (OTW) catheter with a non-compliant balloon. The device is available in diameters of 5 mm to 10 mm and crimped lengths of 16 mm, 22 mm, 38 mm, and 59 mm depending on diameter. See Table 1.

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 80 cm or 120 cm. 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.

The device is provided sterile for one procedure only. Do not resterilize or reuse. Do not use the iCast covered stent system if the sterile package is compromised or the iCast covered stent is damaged. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death.

Table 1 Available Stent Sizes

Diameter (mm)	Length (mm) unexpanded			
	16	22	38	59
5	√	√	√	√
6	√	√	√	√
7	√	√	√	√
8	-	-	√	√
9	-	-	√	√
10	-	-	√	-

Note that the entire iCast covered stent matrix is available in both 80 cm and 120 cm catheter lengths.

2.0 Indication 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.

2.1 Contraindications

The iCast covered stent is contraindicated for use in:

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

2.2 Warnings and Precautions

The device is provided sterile for one procedure only. Do not resterilize or reuse. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death.

1. Caution: Federal (USA) Law restricts this device to sale by or on the order of a physician.
2. Do not use the iCast covered stent system if the box or sterile package is damaged or the iCast covered stent is damaged.
3. People with allergies to 316L stainless steel (in particular nickel) or PTFE may suffer an allergic response to this implant.
4. Do not overlap stents manufactured with differing materials.
5. Use of appropriate anticoagulant and/or antiplatelet therapy per standard of care is recommended for use with this system. Special consideration should be given to patients who have a history of coagulation disorders, contraindications to anticoagulation or antiplatelet

therapy, or contraindications to medications necessary for the procedure.

6. Do not cut the device. The device should only be placed and deployed using the supplied balloon catheter.
7. Clinical experience with the stent has shown that the Arrow International ArrowFlex® Polyurethane Sheath should not be used.
8. Use of the system requires advanced technical skills. Physicians should be trained in interventional techniques such as PTA and placement of intravascular stents. The following instructions will give technical guidance but do not obviate formal training in the use of the device.
9. Do not use air or gaseous medium to inflate the balloon. Significant amounts of air in the balloon may cause uneven expansion of the stent, difficulty in deployment of the stent, or balloon rupture (refer to 3.0 DIRECTIONS FOR USE). Do not preinflate the balloon prior to stent deployment.
10. The 316L stainless steel stent may cause susceptibility artifacts in MRI scans due to distortion of the magnetic field (see 5.0 MRI INFORMATION).
11. Follow the Directions for Use supplied by the manufacturer of any ancillary device used in conjunction with the iCast covered stent system.
12. Do not attempt to reposition or remove a stent once balloon inflation/deployment has been initiated.
13. Do not attempt to withdraw or reposition a balloon catheter within the lumen of the deployed device unless the balloon is completely deflated.
14. Do not remove, reposition or hand crimp the stent.
15. Do not handle or in any way disrupt the placement of the stent on the balloon.
16. Do not expose this device to organic solvents, ionizing radiation or ultraviolet light.
17. The delivery system is not designed for use with power injection systems.
18. Do not force passage or withdrawal of the guidewire through the iCast covered stent system if resistance is encountered.
19. Always consult the label to ensure a compatible sheath is selected for use. Do not force passage or withdrawal of the iCast covered stent and delivery system when interfacing with a sheath or introducer if resistance is encountered. Forcing passage can result in damage to the stent or balloon catheter, stent dislodgment from the balloon, or separation of the catheter components. If using a 10mm device with a Cook introducer sheath, it is recommended to size up to an 8 French sheath to minimize potential for resistance.
20. Prior to balloon inflation, utilize fluoroscopy to verify that the stent has been properly positioned. Do not expand the stent if it is not properly positioned.
21. Balloon pressures are indicated on the product label and should be monitored during inflation. To ensure full stent expansion, inflate to at least the nominal pressure. Do not exceed the rated burst pressure. Use of pressures higher than specified on product label may result in a ruptured balloon with possible vessel damage or perforation.
22. Under-expansion of the stent may result in stent migration.
23. Do not pull an unexpanded stent back through a guiding catheter or sheath (see directions 4.0 REMOVAL OF UNEXPANDED STENT).
24. Stenting across a bifurcation will eliminate or compromise flow and impact future diagnostic or therapeutic procedures.
25. Recrossing a partially or fully expanded stent with adjunct devices must be performed with extreme caution.
26. Do not stent when it is not possible to access the site with standard placement technique.
27. Do not use this device in heavily calcified lesions that are not amenable to PTA or stent placement.

28. Special consideration whether to stent should be given to lesions that contain fresh thrombus, with aneurysms adjacent to site of stent implantation, or with stenosis distal to site of stent implantation.
29. Oversizing of the iCast covered stent and use of higher than recommended inflation pressures may cause dissection.
30. The iCast covered stent is intended to perform as a system. The stent should not be removed for use in conjunction with other dilation catheters, nor should the delivery system be used in conjunction with other stents.
31. Device should not be implanted in patients who have a known active infection at the site of implant.
32. Do not post dilate the iCast covered stent greater than the recommended post dilation diameter (see Table 2 below). Post dilation greater than the recommended diameter may result in the fracture of the stent causing serious injury or death.

Table 2 Maximum Recommended Post-Dilation Diameter (mm)

Labeled Diameter	Device Length			
	16 mm	22 mm	38 mm	59 mm
5	7.3	7.3	9.8	9.8
6	7.3	7.3	10.0	10.0
7	7.3	7.3	10.1	10.1
8	-	-	10.2	10.2
9	-	-	10.4	10.4
10	-	-	10.6	-

33. Use the stent system prior to the 'Use By' date specified on the package.
34. Do not use in locations subject to external compression.

2.3 Potential Hazards and Adverse Events

The following anticipated adverse events (AEs) have been identified as possible complications of endovascular stent implantation in iliac arteries:

- 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

3.0 Directions for Use

General Procedure

1. Patient preparation should be the same as for any angioplasty procedure.
2. Standard techniques for placement of a sheath and guidewire should be employed when using this device.
3. Perform diagnostic angiography to confirm site of implantation and major branch vessels.
4. Evaluate and mark the lesion.

Note: Standard PTA techniques should be used if predilation is necessary.

Sizing

5. Measure the length of the lesion to determine the length of the stent required. The iCast covered stent will foreshorten during deployment. Refer to the stent sizing table (Table 3) listed below and on the product label for the stent length dimensions of the deployed stent. It is recommended to have the stent extend at least 5 mm proximal and distal to the lesion after expansion when possible.

Note: Should more than one stent be required to cover the lesion, place the first stent in the distal segment of the lesion followed by placement of the proximal stent(s). Overlap the stents a minimum of 10 mm for best results.

6. Measure the inner diameter of the vessel to determine the appropriate diameter stent. The iCast covered stent is labeled as the outer diameter. Refer to the stent sizing table (Table 3) listed below and on the product label for the stent OD dimensions of the deployed stent.

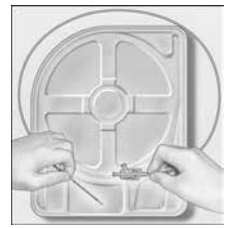
Table 3 Stent Sizing and Foreshortening Based upon Nominal and Burst Pressure

Balloon Diameter (mm)	Stent Length (mm)	Post Nominal Pressure 8 ATM (811 kPa) (mm)		Post Rated Burst Pressure 12 ATM (1216 kPa) (mm)	
		OD	Length	OD	Length
5	16	4.9	15.9	5.2	15.6
5	22	4.9	21.3	5.2	21.0
5	38	5.1	37.2	5.3	37.7
5	59	5.0	58.6	5.3	60.0
6	16	5.7	15.7	6.2	15.1
6	22	5.8	20.8	6.2	20.2
6	38	6.0	36.6	6.3	37.0
6	59	6.0	57.8	6.3	58.7
7	16	6.9	15.0	7.3	14.2
7	22	6.9	20.1	7.3	19.4
7	38	6.9	35.8	7.3	35.7
7	59	7.0	57.1	7.3	57.5
8	38	8.1	34.7	8.5	34.7
8	59	8.0	56.0	8.4	56.5
9	38	8.9	33.7	9.3	32.7
9	59	8.9	54.6	9.3	54.0
10	38	10.0	30.8	10.4	30.9

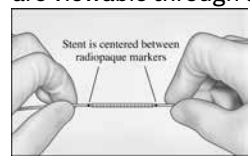
Preparation

Before use, the physician must inspect the iCast covered stent and delivery system in order to ensure that it was not damaged in transport.

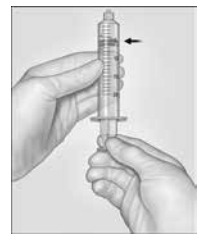
7. Carefully remove the device from the sterile package and ensure the crimped stent or catheter shaft does not come in contact with any non-sterile surfaces or instruments.



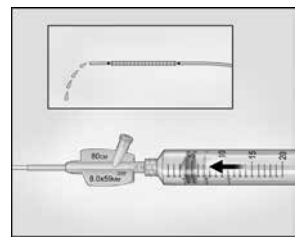
8. Visually inspect the stent to ensure it is centered within the RO markers which are viewable through the folded balloon.



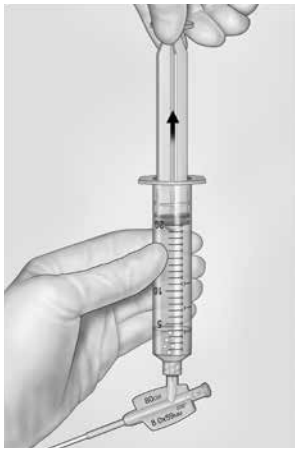
9. Prefill a syringe with sterile saline.



10. Attach the prefilled syringe to the guidewire lumen port as shown (labeled W on the catheter hub) and flush the guidewire lumen until the fluid exits the guidewire exit at the distal tip of the device.



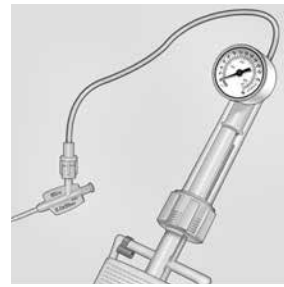
11. Prepare a 20 cc syringe or balloon inflation device with saline or diluted contrast mixture and attach to the balloon inflation port (labeled I on the catheter hub). Hold the delivery system vertical with the distal tip pointing down. Draw back on the syringe applying negative pressure to the catheter and hold for 30 seconds with the syringe in the vertical position.



12. Release the pressure to neutral by gently letting go of the syringe plunger (keeping syringe in an upright position) to allow contrast to fill the delivery catheter inflation lumen(s).

Important: Do not apply positive pressure to the balloon as this can loosen the stent.

13. Repeat steps 11 and 12 at least 3 times until all of the air in the delivery system is expelled. Steps 11 & 12 remove the air from the inflation lumen(s) and balloon, to allow diluted contrast media to fill the inflation lumen(s) to provide more uniform inflation of the balloon during stent deployment.
14. Prepare a 20 cc inflation device equipped with a manometer by filling with 10 cc of diluted contrast media for 5-10 mm diameter balloons. Follow the inflation device instructions. Expel all of the air from the inflation device.
15. Attach the prefilled inflation device to the inflation lumen of the catheter hub (labeled I), ensuring no air bubbles remain at the catheter connection.



16. After the inflation device is connected, confirm the covered stent is between the RO markers. This visual inspection step verifies all preparation steps did not create positive pressure (which could cause inadequate stent deployment) and the stent remains securely positioned within the RO markers prior to patient use.

Deployment

17. Visually inspect the stent for adherence to the balloon and centered placement in relation to the RO markers on the balloon.
18. Confirm that the sheath selected is a compatible size with the selected iCast covered stent system identified on the product label.

Note: Increased resistance may be encountered when inserting a 10mm device through a 7 Fr Cook sheath; therefore, it is recommended to upsize to an 8 Fr sheath

when a Cook sheath is used with a 10mm device.

19. Advance the device over a (0.035") guidewire and through the sheath to the target location under direct fluoroscopic visualization.
20. Utilize fluoroscopy to verify the stent has not shifted or been damaged during positioning. Do not expand the stent if it is not properly positioned.
21. Steadily inflate the balloon to the nominal deployment pressure as stated on the product label.
22. Maintain the inflation pressure for a minimum of 15 seconds at nominal pressure but not greater than burst pressure for full stent expansion.
23. Deflate balloon by pulling vacuum on the inflation device to its maximum volume and allow sufficient time for full deflation.

Note: Deflation times may vary based on balloon size, catheter length, and inflation media used. Deflation may take longer with larger devices and higher concentrations of contrast.

IMPORTANT: Visually verify full deflation of the balloon via fluoroscopy before proceeding to step 24 for withdrawal of the delivery system.

CAUTION: Do not force withdrawal of the delivery system if resistance is encountered. Forcing withdrawal may result in damage to the delivery system, including separation of the balloon or catheter hub from the delivery catheter. If unable to fully deflate the balloon or resistance is encountered, remove the delivery system and introducer sheath/guiding catheter as one unit.

Note: It is recommended that the guidewire remain across the lesion until the procedure is completed.

24. While maintaining guidewire position and negative pressure on the inflation device, slowly withdraw the delivery catheter.
25. Confirm optimal stent apposition using standard angiographic procedures.

3.1 Further Dilation

If necessary, the stent can be post-dilated using standard angioplasty techniques. Maximum iCast covered stent post dilation sizes are listed in Table 2, located in section 2.2 of this IFU.

4.0 Removal of Unexpanded Stent

Extreme caution must be used when removal of an unexpanded or partially expanded stent is necessary. The stent/delivery system should not be withdrawn until the proximal end of the stent is aligned with the distal tip of the introducer sheath. The sheath and the stent delivery system should then all be removed as one unit. After removal, the iCast covered stent system should not be reused.

5.0 MRI Safety Information

Non-clinical testing has demonstrated that the iCast covered stent is MR Conditional. A patient with the iCast covered stent can be scanned safely, immediately after placement, in an MR system meeting the following conditions:

- Static magnetic field of 1.5 T or 3.0 T only.
- Maximum spatial gradient magnetic field of 3,000 gauss/cm (30 T/m).
- Maximum MR system-reported, whole-body averaged specific absorption rate (SAR) of 2 W/Kg (Normal Operating Mode).

Under the scan conditions defined above, the iCast covered stent is expected to produce a maximum temperature rise of 2.2 °C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 15 mm from the iCast covered stent when imaged with a gradient echo pulse sequence and a 3.0 T MRI system. The lumen of the iCast covered stent cannot be visualized on the gradient echo or T1-weighted, spin echo pulse sequence.

6.0 Summary of iCARUS Clinical Study

The iCARUS (iCast covered stent 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. Patients were treated between October 18, 2007 and October 27, 2010. Data was collected through 31 October 2013 and included 165 subjects enrolled from 25 investigational sites. 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. The determination of restenosis was made by direct evaluation of the iliac arteries using duplex ultrasound (or angiography done in lieu of ultrasound). Key secondary endpoints included Major Adverse Vascular Event (MAVE) at each time point through 12 months and Major Adverse Event (MAE) rate at 30 days; device success, acute procedural success, clinical success at each time point through 36 months; patency at each time point 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.

6.1 Patient Population

Patients were required to be at least 18 years of age with lifestyle limiting claudication or rest pain (Rutherford-Becker scale 2-4), and with presence of *de novo* and/or restenotic lesions in the common and/or external iliac artery. Single or multiple target lesions (ipsilateral and/or bilateral), with ≥50% stenosis by visual estimate which could be crossed with a guide wire and dilated, were allowed. Eligible target lesions were between 5 and 12 mm in diameter and <110 mm in length; with evidence of patent profunda or superficial femoral artery (SFA) in the target limb(s). Treatment of non-target lesions in the SFA, meeting certain criteria, was permissible following successful treatment of the target lesion.

To participate in the study, patients were required to give informed written consent, be willing to adhere to the required follow-up visits and testing through month 36 and the required medication regimen following the procedure.

The 165 subjects were enrolled at 24 US sites and 1 German site. Of the 165 subjects enrolled, 13 subjects had inclusion/exclusion violations and were not included in the Intent to Treat (ITT) population.

Subject demographics, medical history and risk factors are summarized in Table 4. The demographics of the study population were typical for this type of study performed in the United States. The iCARUS population was predominantly male (61.8%) with a history of smoking (91.4%), hypertension (84.9%) and hypercholesterolemia (85.5%).

Table 4 Subject Demographics, Medical History and Risk Factors – ITT

	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)

Table 4 Subject Demographics, Medical History and Risk Factors – ITT (Cont'd)

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

* The safety and effectiveness of the iCast covered stent in pediatric populations were not studied in the iCARUS trial. As Peripheral Arterial Disease (PAD) is not typically found in the pediatric population, with the exception of rare homozygous lipid disorders, there is no plan to treat atherosclerotic disease of the common and/or external iliac arteries in this population.

Tables 5 and 6 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±2.1 mm, mean percent stenosis was 69.3±16.7% and mean minimum lumen diameter (MLD) was 2.6±1.5 mm.

Table 5 Angiographic Morphology Data – ITT

Lesion Characteristics	N=152 Lesions = 223
Pre-Procedure Assessment	%(m/n)
Eccentric	49.3% (110/223)
Ulceration	28.7% (64/223)
Totally Occluded	12.1% (27/223)
Calcification	
None/Mild	12.6% (28/33)
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 subjects in the category
n=number of subjects in the study group with sufficient data for analysis

Table 6 Angiographic Quantitative Analysis – ITT

Lesion Characteristics	N=152 Lesions = 223		
	Mean+/-SD	Median	Min-Max
Lesion Length (n=223) (mm)	25.4 ± 16.8	20.4	0.0,90.0
Pre-Procedure Assessment (n=223)			
Reference Vessel Diameter (mm)	8.3± 2.1	8.1	4.1, 16.7
Percent Stenosis (most severe) (%)	69.3 ± 16.7	66.2	26.7, 100.0
Minimum Lumen Diameter (mm)	2.6 ± 1.5	2.7	0.0, 7.9
Post-Procedure Assessment: In stent (n=222)			
Reference Vessel Diameter (mm)	8.4± 2.1	8.1	4.1, 17.0
Percent Stenosis (most severe) (%)	11. 8 ± 9.9	12.4	-21.2, 40.8
Minimum Lumen Diameter (mm)	7.3+1.7	7.1	3.7, 13.1

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

6.2 Methods

Prior to implantation, standard diagnostic angiography was performed to confirm angiographic criteria for the study were met. Lesion length and native vessel diameter were measured in order to select the appropriate length and diameter of the stent(s). Subjects were considered enrolled once the investigational device was entered into the body.

Standard procedures for percutaneous interventional procedures were followed. Pre and post dilation of the lesions were performed at the discretion of the investigator. Concomitant antiplatelet/anti-thrombin and anti-coagulant therapy was administered per routine practice. After the procedure, subjects were prescribed up to 325mg of daily aspirin and 75mg of clopidogrel for 6 months. Ticlopidine could be substituted for subjects with sensitivity to clopidogrel.

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.

6.3 Results

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% CI of 13.4% (p=0.005). This was below the protocol-specified performance goal of 16.57% and the study stent is considered to have met the performance goal (Table 7).

Table 7 Primary Composite Endpoint – ITT

Endpoint	ITT population (N=152)	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%	0.005
Death to 30 days	0.0% (0/151)		
Target Site Revascularization within 9-Months	2.9% (4/139)		
Restenosis at 9-Months	4.9% (6/123)		

Key secondary endpoints included Major Adverse Vascular Events (MAVE) and Major Adverse Events (MAE) as adjudicated by the independent Clinical Events Committee, 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. 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 a procedure related bleeding event requiring transfusion. MAVEs are summarized through 12 months post procedure (Table 8). 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 ≥ 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.

In the ITT population, 4.6% (7/151) of subjects experienced at least one (1) MAVE to 30 days and 6.9% (10/144) of subjects experienced at least one (1) 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 (8) of 151 (5.3%) subjects experienced a MAE to 30 days (seven (7) subjects experienced a MAVE and one (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 (11) subjects that did not achieve acute procedural success, seven (7) subjects experienced an in-hospital MAVE; three

(3) subjects had residual stenosis >30%; and two (2) subjects were documented as device non-success. Note that the eleven (11) subjects includes one (1) subject that experienced both device non-success as well as residual stenosis >30%. One (1) 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%) subjects at all time points through 36 months post-procedure (Table 8). Device, procedural and clinical success results are listed in Table 8.

The composite rate of 30-day death 9-month TSR, and 9-month restenosis in subjects without total occlusions of the iliac was 5% (5/100).

Table 8 Device, Procedural and Clinical Success – ITT

Endpoint	ITT Population (N=152)% (m/n)	95% CI
Major Adverse Vascular Events		
by 30 days	4.6% (7/151)	[1.9%, 9.3%]
by 6-Months	6.9% (10/144)	[3.4%, 12.4%]
by 9-Months	7.1% (10/140)	[3.5%, 12.7%]
by 12-Months	7.2% (10/139)	[3.5%, 12.8%]
Clinical Success		
Early	88.7% (133/150)	[82.5%, 93.3%]
Late by 6-Months	63.5% (80/126)	[54.4%, 71.9%]
Late by 9-Months	76.6% (98/128)	[68.3%, 83.6%]
Late by 12-Months	67.2% (86/128)	[58.3%, 75.2%]
Late by 24-Months	70.8% (80/113)	[61.5%, 79.0%]
Late 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%]

Table 8 Device, Procedural and Clinical Success – ITT (Cont'd)

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%]
Secondary Patency	100.0% (115/115)	[96.8%, 100.0%]
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%]
Major Adverse Events (MAE) at 30-days	5.3% (8/151)	[2.3%, 10.2%]

6.4 Safety Results

A total of 44 of 165 (26.7%) enrolled subjects experienced Serious Adverse Events (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. SAEs that occurred throughout the study for all enrolled subjects are listed in Table 9. Results were similar in the ITT population.

Table 9 Summary of Serious Adverse Events– 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*, Acute myocardial infarction, Angina pectoris, Angina unstable, Atrial fibrillation, Atrial flutter*, Atrioventricular block, Cardiac arrest*, Cardiac failure, Cardiac		

Table 9 Summary of Serious Adverse Events– All Enrolled Subjects (N=165) (Cont'd)

failure congestive, Cardio-respiratory arrest, Coronary artery disease, Coronary artery occlusion*, Myocardial infarction, Stress cardiomyopathy*, Ventricular tachycardia)	13(7.9%)	33(20.0%)
Ear and Labyrinth Disorders (Vertigo*)	0	1(0.6%)
Gastrointestinal Disorders (Abdominal pain*, Colitis*, Gastritis*, Gastrointestinal haemorrhage, Intestinal obstruction*, Intestinal perforation, Nausea*, Pancreatitis*, Pancreatitis acute*, Peritonitis*, Rectal haemorrhage*, Small intestine obstruction*, Upper gastrointestinal haemorrhage, Vomiting*)	5(3.0%)	13(7.9%)
General Disorders and Administration Site Conditions (Asthenia, Catheter site haematoma, Chest pain, Impaired healing*, Non-cardiac chest pain*)	6(3.6%)	10(6.1%)
Hepatobiliary Disorders (Cholecystitis*, Hepatic steatosis*)	0	2(1.2%)
Immune System Disorders (Anaphylactic reaction)	1(0.6%)	2(1.2%)
Infections and Infestations (Abdominal abscess, Bronchitis*, Bronchitis bacterial*, Cellulitis*, Gastroenteritis viral*, Groin abscess*, Influenza*, Pneumonia, Pneumonia staphylococcal*, Post procedural sepsis*, Sepsis, Urosepsis*)	6(3.6%)	18(10.9%)
Injury, Poisoning, and Procedural Complications (Abdominal wound dehiscence*, Anaemia postoperative*, Aortic injury*, Arterial injury, Device dislocation*, Femur fracture, In-stent arterial restenosis, Incisional hernia*, Postoperative ileus*, Spinal fracture*, Stent occlusion*, Subdural haematoma, Tendon injury*, Traumatic brain injury*, Urostomy complication*, Vascular graft occlusion*)	5(3.0%)	19(11.5%)
Metabolism and Nutrition Disorders (Acidosis*, Fluid overload*, Hyperkalaemia*, Hypoglycaemia, Hyponatraemia, Obesity*)	2(1.2%)	6(3.6%)
Musculoskeletal and Connective Tissue Disorders (Arthralgia*, Arthritis, Fistula*, Muscular weakness*, Osteoarthritis, Rhabdomyolysis*)	2(1.2%)	7(4.2%)
Neoplasm Benign, Malignant, and Unspecified (cysts and polyps) (Bronchial carcinoma*, Colon cancer, Colon cancer recurrent*, Hepatic neoplasm malignant*, Lung cancer metastatic, Lung neoplasm malignant, Lymphoma*, Metastases to liver, Prostate cancer*, Transitional cell carcinoma*)	3(1.8%)	9(5.5%)
Nervous System Disorders (Brain mass*, Carotid artery stenosis, Cerebrovascular accident, Encephalopathy, Polyneuropathy*, Subarachnoid haemorrhage, Syncope, Syncope vasovagal*, Transient ischaemic attack)	7(4.2%)	14(8.5%)
Psychiatric Disorders (Depression)	1(0.6%)	1(0.6%)
Renal and Urinary Disorders (Calculus ureteric*, Renal artery occlusion*, Renal artery stenosis*, Renal disorder*, Renal failure*, Renal failure acute, Renal failure chronic, Renal mass*)	2(1.2%)	13(7.9%)
Reproductive System and Breast Disorders (Galactorrhoea*)	0	1(0.6%)
Respiratory, Thoracic, and Mediastinal (Acute respiratory failure*, Chronic obstructive pulmonary disease*, Dyspnoea*, Epistaxis, Pleural effusion*, Pneumonia aspiration, Pneumothorax*, Pulmonary embolism*, Pulmonary mass*, Pulmonary oedma, Respiratory failure*)	2(1.2%)	10(6.1%)
Skin and Subcutaneous Tissue Disorders (Psoriasis*, Skin ulcer*)	0	2(1.2%)
Vascular Disorders (Aortic stenosis*, Arterial restenosis, Arterial thrombosis limb, Femoral arterial stenosis, Femoral artery occlusion, Haemorrhage*, Hypotension, Iliac artery stenosis, Intermittent claudication, Orthostatic hypotension, Peripheral arterial occlusive disease, Peripheral artery aneurysm*, Peripheral ischaemia*, Peripheral vascular disorder*, Subclavian artery stenosis, Vascular pseudoaneurysm)	14(8.5%)	30(18.2%)

*Preferred Term applies to events to 36 months only

System Organ Class	Preferred Term	Subjects with events to 9 months	Subjects with events to 36 months

6.5 Conclusion

This prospective, multi-center, single-arm clinical trial (iCARUS) has demonstrated that the iCast covered stent 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 to a predetermined performance goal. 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% as compared to the performance goal of 16.57% (p=0.005). As this is significantly below the performance goal of 16.57%,

the trial met its primary composite endpoint. 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 covered stent.

The benefits of stenting with the iCast covered stent 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 when used for revascularization of iliac artery lesions. These results were consistent with clinical results from the COBEST study.*** Altogether, these data support the safety and effectiveness of the iCast covered stent when used for revascularization of iliac lesions in the studied patient population.

***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.

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.

Symbols Used On Product Labels

KEEP AWAY FROM SUNLIGHT KEEP DRY DO NOT RESTERILIZE DO NOT RE-USE

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DO NOT USE IF PACKAGE IS DAMAGED STERILE EO STERILIZED USING ETHYLENE OXIDE

REF CATALOGUE NUMBER SN SERIAL NUMBER DIM DIMENSIONS QTY BOX QUANTITY

CONSULT INSTRUCTIONS FOR USE

Rx Only CAUTION: FEDERAL LAW (U.S.A.) RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN

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Printed in U.S.A. • Part No. 009603 AW009603-EN Rev AA • 2023-04