VENOVO®

Venous Stent System

Instructions for Use

BARD | PERIPHERAL VASCULAR

B05886 Rev.0/08-18

Instructions for Use

1. Device Description

The VENOVO® Venous Stent System is designed to deliver a self-expanding stent to the peripheral venous vasculature via a sheathed delivery system. The VENOVO® Venous Stent System is comprised of the following:

- An implantable self-expanding nitinol (nickel-titanium) alloy stent (Figure 1) designed for the treatment of symptomatic iliofemoral venous outflow obstruction. The stent is a flexible, fine tubular mesh prosthesis which achieves its unconstrained diameter upon deployment into the target vessel. Upon deployment, the stent imparts an outward radial force on the luminal surface of the vessel to establish patency. The stent has a total of 12 markers located on the ends of the stent, six at each end. Three at each end are radiopaque tantalum markers (1A) and three are made out of nitinol (nickel-titanium) (1B).

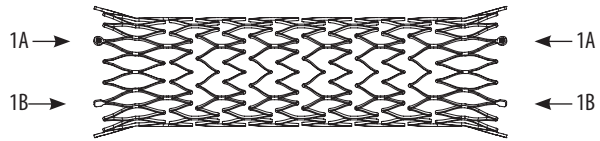


Figure 1: VENOVO® Venous Stent

Figure 2: VENOVO® Venous Stent System

- A triaxial, over-the-wire delivery system (Figure 2) comprised of an inner tubing assembly that contains the guidewire lumen, a stent delivery sheath (D + E) and a system stability sheath (C), which are linked together by a handle. The guidewire lumen originates proximally with a Luer hub (B) and terminates distally with a catheter tip (A). The guidewire lumen is designed to accept a compatible 0.035 inch guidewire.

  The self-expanding stent is constrained in the space between the guidewire lumen and the stent delivery sheath. Unintended stent movement during sheath retraction is restricted by the delivery system. Prior to deployment, the safety lock slider (F) must be unlocked. Deployment of the stent is initiated by rotating the large thumbwheel (G) on the handle. The distal catheter will retract using either the large thumbwheel for slow deployment of the stent or the small thumbwheel (H) for faster deployment of the stent.

2. Indication for Use

The VENOVO® Venous Stent System is indicated for the treatment of symptomatic iliofemoral venous outflow obstruction.

3. Contraindications

The VENOVO® Venous Stent System is contraindicated for use in:

- Patients with a known hypersensitivity to nitinol (nickel-titanium) and tantalum.
- Patients who are judged to have a lesion that prevents complete inflation of a balloon dilatation catheter or proper placement of the stent or the stent delivery system.
- Patients who cannot receive intraprocedural anti-coagulation therapy.

4. Warnings

- The VENOVO® Venous Stent System is supplied **STERILE** and is intended for **SINGLE USE ONLY. DO NOT RESTERILIZE** and/or **REUSE** the device.
  Reuse, resterilization, reprocessing and/or repackaging may create a risk to the patient or user, may lead to infection or compromise the structural integrity and/or essential material and design characteristics of the device, which may lead to device failure, and/or lead to injury, illness, or death of the patient.
  Reusing this medical device bears the risk of cross-patient contamination as medical devices – particularly those with long and small lumina, joints, and/or crevices between components – are difficult or impossible to clean once body fluids or tissues with potential pyrogenic or microbial contamination have had contact with the medical device for an indeterminable period of time. The residue of biological material can promote the contamination of the device with pyrogens or microorganisms which may lead to infectious complications or death.
- DO NOT use in patients with total venous occlusion that cannot be dilated to allow passage of the guidewire.
- DO NOT use the device with contralateral access.
- DO NOT use if pouch is opened or damaged.
- DO NOT use the device after the "Use By" date specified on the label.
- Persons with allergic reactions to nitinol (nickel-titanium) alloy and/or tantalum may suffer an allergic response to this implant.
- DO NOT expose the delivery system to organic solvents, e.g., alcohol.
- The stent is not designed for repositioning or recapturing.
- Stenting across a major branch could cause difficulties during future diagnostic or therapeutic procedures.
- If a long lesion needs to be stented consider using the longest available stent rather than overlapping stents. If multiple stents are placed in an overlapping fashion, they should be of similar composition (i.e., nitinol).
- The long-term outcomes following repeat dilatation of endothelialized stents are unknown.
- The safety and effectiveness of this device for use in the arterial system have not been established.

5. Precautions

- The device is intended for use by physicians who have received appropriate training.
- During system flushing, observe that saline exits at the catheter tip.
- The delivery system is not designed for use with power injection systems.
- Recrossing a partially or fully deployed stent with adjunct devices must be performed with caution.
- Prior to stent deployment, remove slack from the delivery system catheter outside the patient.
- If excessive force is felt during stent deployment, do not force the delivery system. Remove the delivery system and replace with a new unit.
- Store in a cool, dark, dry place.
- Do not attempt to break, damage, or disrupt the stent after placement.

6. Magnetic Resonance Imaging (MRI) Compatibility

MR

Non-clinical testing has demonstrated that the VENOVO® Venous Stent is MR Conditional for single and overlapping placement in the iliac and femoral veins for all clinically relevant lengths. Based upon the preclinical testing, patients with the VENOVO® Venous Stent can be scanned safely, immediately after placement of this implant, under the following conditions:

- Static magnetic field of 1.5 Tesla or 3.0 Tesla only.
- Spatial gradient field of 3000 Gauss/cm or less.
- Maximum whole-body-averaged specific absorption rate (SAR) of 2 W/kg for 15 minutes of scanning for landmark above umbilicus and 1 W/kg for landmark below umbilicus.

3.0 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 10 x 80 mm VENOVO® Venous Stent was determined to produce a potential worst-case temperature rise of 5.2 °C at the whole body SAR limits stated above for 15 minutes of MR scanning in a 3.0 Tesla whole body MR system. Cooling due to blood flow inside the stent and perfusion in the vascular bed surrounding the stent was included in the assessment of in-vivo temperature rise.

1.5 Tesla Temperature Rise

In an analysis based on non-clinical testing according to ASTM F2182-11a and computer modeling of a patient, the 10 x 160 mm VENOVO® Venous Stent was determined to produce a potential worst-case temperature rise of 3.4 °C at the whole body SAR limits stated above for 15 minutes of MR scanning in a 1.5 Tesla whole body MR system. Cooling due to blood flow inside the stent and perfusion in the vascular bed surrounding the stent was included in the assessment of in-vivo temperature rise.

Image Artifact

MR image quality may be compromised if the area of interest is in the exact same area or relatively close to the position of the stent. Artifact tests were performed according to ASTM F2119-07. Maximum artifact extended 22 mm beyond the stent for the spin echo sequence and 5 mm for the gradient echo sequence. The lumen was obscured.

Additional Information

The VENOVO® Venous Stent has not been evaluated in MRI systems with field strengths other than 1.5 or 3.0 Tesla. The heating effect in the MRI environment for fractured stents is not known. The presence of other implants or the health state of the patient may require reduction of the MRI limits listed above.

7. Potential Complications and Adverse Events

Complications and Adverse Events which may occur include, but are not limited to, the following:

- Allergic/anaphylactic reaction
- Amputation
- Aneurysm
- Arteriovenous fistula
- Death related to procedure
- Death unrelated to procedure
- Dissection
- Embolization, venous
- Embolization, stent
- Extravasation
- Fever
- Hemorrhage/bleeding requiring a blood transfusion
- Hematoma, remote site
- Hematoma, puncture site
- Hypotension/hypertension
- Incorrect positioning of the stent requiring further stenting or surgery
- Intimal injury/dissection
- Ischemia/infarction of tissue/organ
- Local infection
- Malposition (failure to deliver the stent to the intended site)
- Open surgical repair
- Pain
- Pulmonary embolism
- Pseudoaneurysm
- Renal failure
- Respiratory arrest
- Restenosis
- Rupture
- Septicemia/bacteremia
- Stent Fracture
- Stent Migration
- Vasospasm
- Venous occlusion/thrombosis, remote from puncture site
- Venous occlusion/thrombosis, near the puncture site
- Venous occlusion/restenosis of the treated vessel

8. How Supplied

The Venovo® Venous Stent System is supplied sterile (by ethylene oxide) and is nonpyrogenic. Do not resterilize and/or reuse this device. Do not use if pouch is opened or damaged. Do not use the device after the "Use By" date specified on the label.

Contents

- One (1) Venovo® Venous Stent System
- One (1) Patient Implant Information Card

Patient Implant Information Card

A Patient Implant Information Card is provided within the product packaging. The patient, implant and hospital information should be recorded on the card. Ensure a peel-away sticker from the product label is placed on the card before it is given to the patient. The sticker contains important information about the implant. The patient should carry the implant information card with them and present it to any medical personnel involved in their care.

Storage

Store in a cool, dry place. Keep away from sunlight. Use the device prior to the "Use By" date specified on the package.

Disposal

After use, the delivery system is a potential biohazard. Handle and dispose of it in accordance with accepted medical practice and applicable local, state and federal laws and regulations.

9. Directions for Use

9.1 Pre-Deployment Procedure

9.1.1 Inject Contrast Media

- Perform a venogram using standard technique.

9.1.2 Evaluate and Mark Target Site

- Fluoroscopically evaluate and mark the target site observing the most obstructed segment.

9.1.3 Select Stent Size

- Measure the length of the target lesion to identify the appropriate length of stent(s) required. Ensure that the stent is long enough to permit the area proximal and distal of the lesion to be covered by the stent.
- The stent dimensions listed in Table 1 include the smallest and largest stent sizes offered. The results provided are indicative of the foreshortening for the entire stent size matrix.

Table 1: Stent Foreshortening Table

Stent Foreshortening Table					
Stent Size (mm)	**Vessel Diameter [mm]**	**Foreshortening [%]***			**Percent Stent Free Area** (% at max to min oversizing)
		Min	**Mean**	**Max**	
10×40	7-9	-3	2	5	80-85
10×160		-2	1	3	
12×40	9-11	-4	3	6	84-87
12×160		0	2	4	
14×40	11-13	1	4	7	85-87
14×160		0	1	1	
16×40	13-15	1	4	5	84-87
16×160		-3	1	3	
18×40	15-17	3	6	9	84-86
18×160		1	2	4	
20×40	17-19	2	7	10	86-87
20×160		-2	2	6	

* Values based on mathematical calculations.

- Identify the diameter of the reference vessel (proximal and distal to the lesion). To ensure secure placement, refer to the stent size selection table for proper sizing scheme (Table 2). Refer to product labeling for stent length.

Table 2: Stent Size Selection Table

Stent Size Selection Table	
Reference Vessel Diameter	**Unconstrained Stent Inner Diameter**
7 - 9 mm	10 mm
9 - 11 mm	12 mm
11 - 13 mm	14 mm
13 - 15 mm	16 mm
15 - 17 mm	18 mm
17 - 19 mm	20 mm

9.1.4 Materials Required

In addition to the VENOVO® Venous Stent System, the following standard materials may also be required to facilitate delivery and deployment of the VENOVO® Venous Stent System:

- Normal, sterile saline
- Sterile syringes
- 8F introducer for stent diameters of 10 mm and 12 mm
- 9F introducer for a stent diameter of 14 mm
- 10F introducer for stent diameters of 16 mm, 18 mm and 20 mm
- 0.035 inch diameter guidewire
- Balloon dilatation catheter
- Intravenous contrast medium diluted with normal, sterile saline
- Inflation device
- Appropriate anticoagulation drugs

9.1.5 Prepare Stent System

- Open the box and remove the pouch containing the stent system.
- Carefully inspect the pouch for damage to the sterile barrier. Do not use after the expiration date. Peel open the pouch and remove the tray containing the stent system. Carefully extract the stent system from the tray.
- Check the following:
  - Verify that the safety lock slider is still in the locked position (Figure 3).

Safety lock slider in locked position | Safety lock slider in unlocked position

Figure 3: Handle top view

- Examine the stent system for any damage. If it is suspected that the sterility or performance of the stent system has been compromised, the device must not be used.
- Visually inspect the distal end of the stent system to ensure that the stent is contained within the sheath. Do not use if the stent is partially deployed.
- Prior to use flush the guidewire lumen of the stent system with normal, sterile saline until saline exits the tip of the system (Figure 4).

Figure 4: System flushing

- Wipe the usable length portion of the stent system with gauze soaked with normal, sterile saline.

9.2 Stent Deployment Procedure

9.2.1 Insert Introducer Sheath and Guidewire

- Gain femoral, popliteal or jugular access utilizing an appropriate introducer sheath. See "Materials Required" Section.
- For jugular access, use the stent system in conjunction with a long introducer sheath that covers the right atrium.
- Insert a guidewire of appropriate length (Table 3) and 0.035 inch diameter across the lesion to be stented via the introducer sheath.

Table 3: Recommended Guidewire Length Table

Recommended Guidewire Length Table	
Catheter Working Length	**Recommended Guidewire Length**
120 cm	300 cm
80 cm	200 cm

9.2.2 Dilate Lesion

- Predilation of chronic lesions with a balloon dilatation catheter is recommended. If performed, select a balloon catheter that matches the size of the reference vessel.
  Caution: During dilation, do not expand the balloon such that dissection complication or perforation could occur.
- While maintaining site access with a guidewire, remove the balloon catheter from the patient.

9.2.3 Introduce Stent System

- Advance the stent system over the guidewire through the introducer sheath.
  Note: If resistance is met during stent system introduction, the stent system should be withdrawn and another stent system should be used.
  Caution: Always use an introducer sheath for the implant procedure to protect the vasculature and the puncture site.
- Position the tip of the stent system past the target site.
- Remove slack from the stent system held outside the patient.
  Caution: Any slack in the stent system (outside the patient) could result in deploying the stent beyond the target site.

9.2.4 Deploy Stent

- Confirm that the introducer sheath is secure and will not move during deployment.
- Unlock the safety lock slider by pulling it back towards the wheels from the locked position into the unlocked position. Ensure that the red safety lock slider is completely pulled back (Figure 5).

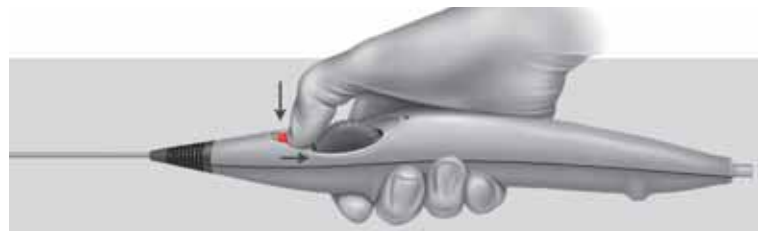


Figure 5: Unlock safety lock slider

- Pull back the stent system until the distal and proximal stent radiopaque markers are in position so that they are distal and proximal to the target site.
- The second hand should be used to support the stent delivery system. Gently hold the stability sheath and maintain it straight and under tension throughout the procedure (Figure 6).
- **DO NOT** hold or touch the dark moving sheath during stent release (Figure 7).

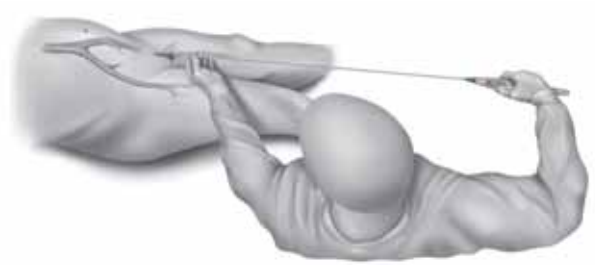


Figure 6: Hold system straight

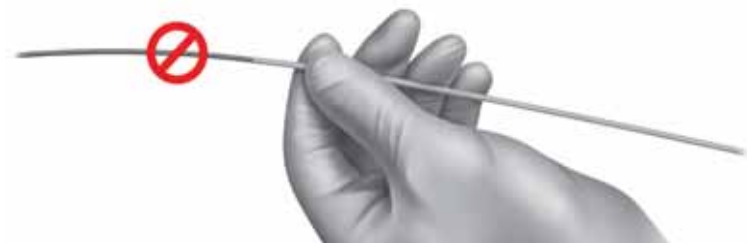


Figure 7: Hold stability sheath. **DO NOT** hold or touch the dark moving sheath.

Note: Do NOT constrict the delivery system during stent deployment. If excessive force is felt during stent deployment, do not force the stent system. Remove the stent system and replace with a new unit.

- Initiate stent deployment by rotating the large thumbwheel in the direction of the arrows while holding the handle in a fixed position.

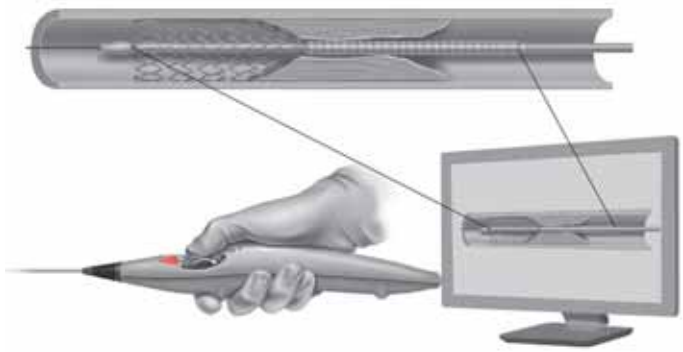


Figure 8: Stent release

- While using fluoroscopy, maintain position of the distal and proximal stent radiopaque markers relative to the targeted site.
- Watch for the distal stent radiopaque markers to begin separating; separation of the distal stent radiopaque markers signals that the stent is deploying. Continue turning the large thumbwheel until the distal end of the stent obtains complete wall apposition (Figure 8).
- With the distal end of the stent apposing the vessel wall, final deployment can be continued, depending on user preference, with rotating the small or the large thumbwheel.
- Deployment of the stent is complete when the proximal stent radiopaque markers appose the vessel wall. **DO NOT** attempt to recapture the stent.

9.3 Post Stent Placement

- Remove the delivery system from the body.

  Note: If resistance is met while retracting the delivery system over a guidewire, remove the delivery system and guidewire together.

- Post stent expansion with a balloon dilatation catheter is recommended. If performed, select a balloon catheter that matches the size of the reference vessel, but that is not larger than the stent diameter itself.
- Remove the guidewire and introducer sheath from the body.
- Close entry wound as appropriate.
- Discard the delivery system, guidewire and introducer sheath following institutional procedures.

Note: Physician experience and discretion will determine the appropriate antithrombotic drug regimen for each individual patient.

10. Summary of Clinical Study

The Venovo® Venous Stent System was evaluated through an Investigational Device Exemption (IDE) study in the prospective, multi-center, non-randomized, single-arm, VERNACULAR study for the treatment of symptomatic iliofemoral venous outflow obstruction. Effectiveness and safety measures of subjects receiving the Venovo® Venous Stent are presented with information derived from clinical literature.

A total of 231 subjects were consented and screened for eligibility. Of these, 170 were treated with the Venovo® Venous Stent at 22 investigational sites in the United States, Europe and Australia, of which 21 remain active. The most common reason for exclusion from the study was failure to meet the criteria associated with symptomatic venous outflow obstruction of ≥ 50% as measured by catheter contrast venography. The endpoint analyses were conducted on subjects who had reached pre-specified follow-up time points: 30 days for primary safety and 12 months for effectiveness. Subjects will be followed through 36 months.

Study Endpoints

For this study, the primary effectiveness endpoint and primary safety endpoint are considered co-primary endpoints. The primary effectiveness endpoint of the study is primary patency at 12 months post-index procedure, defined as freedom from target vessel revascularization (TVR); freedom from thrombus occlusion and stenosis > 50% as measured by duplex ultrasound (DUS). TVR is defined as the first revascularization procedure of the target vessel as determined by an Independent Core Lab. The primary effectiveness endpoint was evaluated against a literature-derived performance goal (PG) of 74%, which was set at 10% below the weighted mean of primary patency (PP) rate at 12 months at a combination of 55% Post-Thrombotic Syndrome (PTS) subjects at PP rate of 77.1% and 45% non-thrombotic iliac vein lesion (NIVL) subjects at PP rate of 93.4%. The primary safety endpoint of the study is freedom from major adverse events (MAE) through 30 days post-index procedure, defined as the following: TVR; device and/or procedure-related death; target limb major amputation; pulmonary embolism which is clinically important (symptomatic with chest pain, hemoptysis, dyspnea, hypoxia, etc.); vascular injury requiring surgical/endovascular intervention; embolization/migration of stent; device- and/or procedure-related acute DVT involving the treated limb. The primary safety endpoint was evaluated against a PG of 89%, which was set at 10% below the literature-derived average freedom from MAE rate at 30 days of 99%.

The following secondary endpoints were evaluated (and will be evaluated at the 24- and 36-month intervals that have not yet occurred) to provide further information related to the safety and effectiveness of the Venovo® Venous Stent:

- Venous Clinical Severity Score (VCSS) at 30 days, 6-, 12- (hypothesis tested for pain score at 12 months), 24-, and 36-months and at any target lesion revascularization (TLR) or TVR.
- Quality of Life (QoL) Chronic Venous Insufficiency Questionnaire (CIVIQ-20) at baseline, 30-days and 6-, 12- (hypothesis tested), 24- and 36-months post-index procedure and at any TLR/TVR.
- CEAP score at 30 days, 6- 12-, 24-, and 36-months and at any TLR/TVR.
- Acute Technical Success defined as successful deployment of stent(s) to intended target with adequate lesion coverage as assessed by the Investigator.
- Acute Procedure Success defined as technical success with no MAE between index procedure and discharge.
- Lesion Success defined as attainment of ≤ 50% residual stenosis (from core lab) at the conclusion of the index procedure.
- Freedom from TLR at 30 days, 6-, 12-, 24-, and 36-months post-index procedure.
- Freedom from TVR at 30 days, 6-, 12-, 24-, and 36-months post-index procedure.
- Primary patency at 24- and 36-months.
- X-ray analysis of stent fracture at 12-, 24-, and 36-months.

For sample size determinations, this study was projected to include up to one-hundred seventy (170) subjects treated with the Venovo® Venous Stent. The sample size was estimated to give adequate power on the two co-primary endpoints (primary patency at 12 months and freedom from MAE rate at 30 days post-index procedure).

Subjects Studied

To be included in the study, eligible subjects were required to be male or non-pregnant female ≥ 18 years of age with symptomatic (non-malignant) venous outflow obstruction in iliofemoral venous segments of ≥ 50% as determined by catheter contrast venography. Required reference vessel diameters needed to be between 7 mm and 19 mm as determined by the Investigator's visual estimate. Additionally, eligible subjects needed to have a CEAP "C" ≥ 3 or a VCSS pain score of ≥ 2. Subjects were not permitted to enroll in the VERNACULAR study if they did not meet the venous outflow obstruction requirement for the target vessel, had a malignant obstruction, were asymptomatic and had a CEAP "C" < 3, or a VCSS pain score of < 2. Although not specified in the selection criteria but specified in the protocol, the use of up to two (2) Venovo® Venous Stents (placed in an overlapping fashion) was acceptable in this study. The recommended overlap of the two (2) Venovo® Venous Stents was suggested to be approximately 10 mm.

Methods

All treated subjects underwent a clinical evaluation at the index procedure as well as at hospital discharge. Clinical follow-up for treated subjects was performed at hospital discharge, 30 days, 6 months, and 12 months post-index procedure and will continue through 24 and 36 months post-index procedure. Pre-dilatation was not required per the protocol and was completed for 132 subjects (77.6% of the target lesions). Post-dilatation was not required per the protocol and was performed in 154 subjects (90.6% of the target lesions).

All data were collected on case report forms at investigational sites. Adverse events were adjudicated by the clinical events committee (CEC), and the data safety monitoring board (DSMB) routinely reviewed the study outcomes to ensure that the benefits of continuing the study outweighed any potential risks. An independent CEC reviewed all adverse events (AEs) and performed adjudications of events in accordance with their charter.

Results

SUBJECT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Tables 4 - 7 summarize the intent-to-treat (ITT) subject demographics, medical history, baseline characteristics, target lesions treated, and study device details.

Table 4: Subject Demographics

	PTS N = 93	NIVL N = 77	Total N= 170
Age Categories	**n (%)**	**n (%)**	**n (%)**
< 65 years	77 (82.8)	48 (62.3)	125 (73.5)
≥ 65	16 (17.2)	29 (37.7)	45 (26.5)
Sex	**n (%)**	**n (%)**	**n (%)**
Male	42 (45.2)	21 (27.3)	63 (37.1)
Female	51 (54.8)	56 (72.7)	107 (62.9)
Ethnicity	**n (%)**	**n (%)**	**n (%)**
Hispanic or Latino	7 (7.5)	5 (6.5)	12 (7.1)
Not Hispanic or Latino	86 (92.5)	72 (93.5)	158 (92.9)
Race	**n (%)**	**n (%)**	**n (%)**
Asian	3 (3.2)	1 (1.3)	4 (2.4)
Black or African American	7 (7.5)	2 (2.6)	9 (5.3)
White	83 (89.2)	73 (94.8)	156 (91.8)
Other	0	1 (1.3)	1 (0.6)
BMI (kg/m^2)			
N	93	76	169
Mean (SD)	28.57 (6.36)	29.12 (7.65)	28.82 (6.95)
Median	27.10	28.30	27.40
Min-Max	18.2 – 49.1	18.2 – 50.0	18.2 – 50.0
Disease Category	**n (%)**	**n (%)**	**n (%)**
PTS	93 (100.0)	0	93 (54.7)
NIVL	0	77 (100.0)	77 (45.3)
Number of Target Lesions	**n (%)**	**n (%)**	**n (%)**
1	81 (87.1)	73 (94.8)	154 (90.6)
2	12 (12.9)	4 (5.2)	16 (9.4)

Table 5: Medical History

Cardiovascular Disease	PTS N= 93 n (%)	NIVL N= 77 n (%)	Total N= 170 n (%)
Subjects with any Cardiovascular Disease	**93 (100.0)**	**77 (100.0)**	**170 (100.0)**
Stroke	2 (2.2)	2 (2.6)	4 (2.4)
Angina	3 (3.2)	2 (2.6)	5 (2.9)
Hypertension	27 (29.0)	28 (36.4)	55 (32.4)
Coronary Artery Disease (CAD)	6 (6.5)	9 (11.7)	15 (8.8)
Myocardial Infarction (MI)	3 (3.2)	3 (3.9)	6 (3.5)
Transient Ischemic Attack (TIA)	2 (2.2)	1 (1.3)	3 (1.8)
Cardiomyopathy	2 (2.2)	1 (1.3)	3 (1.8)
Vascular Heart Disease	1 (1.1)	1 (1.3)	2 (1.2)
Deep Vein Thrombosis (DVT)	92 (98.9)	0	92 (54.1)
May-Thurner Syndrome	35 (37.6)	67 (87.0)	102 (60.0)
Venous Valve Disease	7 (7.5)	5 (6.5)	12 (7.1)
Varicosis	71 (76.3)	62 (80.5)	133 (78.2)
Dyslipidemia	20 (21.5)	27 (35.1)	47 (27.6)
Peripheral Arterial Disease (PAD)	6 (6.5)	12 (15.6)	18 (10.6)
Atrial Fibrillation (A-FIB)	4 (4.3)	2 (2.6)	6 (3.5)
Arrhythmia (Other Than A-FIB)	3 (3.2)	5 (6.5)	8 (4.7)
Other	19 (20.4)	24 (31.2)	43 (25.3)
Renal Disease	**n (%)**	**n (%)**	**n (%)**
Subjects with any renal disease	7 (7.5)	3 (3.9)	10 (5.9)
Chronic Kidney Disease	2 (2.2)	2 (2.6)	4 (2.4)
Acute Renal Insufficiency (Serum Creatinine Greater Than or Equal to 2.5 mg/dL)	1 (1.1)	0	1 (0.6)
Uremia	1 (1.1)	0	1 (0.6)
Other	5 (5.4)	2 (2.6)	7 (4.1)
Other Disease	**n (%)**	**n (%)**	**n (%)**
Subjects with any other disease	72 (77.4)	64 (83.1)	136 (80.0)
Diabetes	5 (5.4)	13 (16.9)	18 (10.6)
Bleeding Disorder	7 (7.5)	0	7 (4.1)
Cancer	6 (6.5)	8 (10.4)	14 (8.2)
Gastrointestinal Disease	11 (11.8)	7 (9.1)	18 (10.6)
Genitourinary Disorder	5 (5.4)	3 (3.9)	8 (4.7)
Respiratory Disorder	13 (14.0)	7 (9.1)	20 (11.8)
Liver Disease	4 (4.3)	2 (2.6)	6 (3.5)
Systemic Lupus Erythematosus	2 (2.2)	0	2 (1.2)
Cigarette Smoking	28 (30.1)	30 (39.0)	58 (34.1)
Allergic Reaction, Sensitivity, or Intolerance to Nickel or Titanium, Contrast Media, Antiplatelet, Anticoagulant or Thrombolytic Medications	3 (3.2)	5 (6.5)	8 (4.7)
Other	60 (64.5)	54 (70.1)	114 (67.1)

Note: A subject may take multiple medication

At the time of the analysis, the 170 subjects were treated with VENOVO® Venous Stent. Table 6 shows the lesion characteristics that were treated.

Table 6: Summary of Target Lesions

	PTS	NIVL	Total
Target Limb	**n/N (%)**	**n/N (%)**	**n/N (%)**
Right Leg	18/89 (20.2)	8/74 (10.8)	26/163 (16.0)
Left Leg	71/89 (79.8)	66/74 (89.2)	137/163 (84.0)
Target Lesion Location	**n/N (%)**	**n/N (%)**	**n/N (%)**
Common Iliac	82/89 (92.1)	72/74 (97.3)	154/163 (94.5)
External Iliac	52/89 (58.4)	14/74 (18.9)	66/163 (40.5)
Common Femoral	13/89 (14.6)	2/74 (2.7)	15/163 (9.2)
Lesion Length (mm)			
N	73	73	146
Mean (SD)	80.52 (42.78)	55.15 (31.99)	67.84 (39.74)
Median	71.18	45.40	56.17
Minimum–Maximum	18.05 – 199.66	22.13 – 183.44	18.05 – 199.66

Note: A subject may have multiple target lesion locations.

Table 7: Study Device Details

	PTS N = 93	NIVL N = 77	Total N = 170
Stent Diameter (mm)			
Mean (SD)	15.4 (2.09)	16.6 (1.99)	15.9 (2.12)
Median	16.0	16.0	16.0
Min - Max	10 - 20	12 - 20	10 - 20
Stent Length (mm)			
Mean (SD)	100.1 (33.15)	83.0 (26.33)	93.5 (31.74)
Median	100.0	80.0	80.0
Min - Max	40 - 160	40 - 160	40 - 160
Device Used to Treat Study Subject?	n/N (%)	n/N (%)	n/N (%)
Yes	134/136 (98.5)	85/87 (97.7)	219/223 (98.2)
No	2/136 (1.5)	2/87 (2.3)	4/223 (1.8)

Subject Accountability

Overall, 231 subjects were consented into the VERNACULAR study. One hundred and seventy (170) subjects were treated with the study device and formed the Intent-to-Treat (ITT) population. Of the sixty-one (61) subjects which were enrolled but not treated, fifty-eight (58) subjects did not meet the inclusion/exclusion criteria as defined above and were considered screen failures. The remaining three (3) subjects met all eligibility criteria but were not treated with the study device: one (1) subject was consented but could not be treated prior to completion of overall enrollment of the study, and two (2) subjects were enrolled in a different device trial at the discretion of the investigator. One hundred and fifty-six (156) subjects were available for the effectiveness analysis at 12-months as of July 17, 2018 (date of database lock). Of the fourteen (14) subjects that did not have a 12-month follow-up, three (3) subjects withdrew consent, four (4) subjects died, three (3) subjects were lost to follow-up, and four (4) subjects missed the 12-month visit with the following caveat. Five (5) subjects missed the 12-month follow-up visit. One (1) subject was lost to follow-up at day 398 and is therefore accounted for in the lost to follow-up total and not the missed visit total. The death events were adjudicated by the CEC and determined to not be related to the study device or procedure.

Summary of Effectiveness

The primary effectiveness endpoint of the study was primary patency at 12 months post-index procedure. The primary effectiveness endpoint was evaluated against a literature-derived PG of 74%, which was set at 10% below the weighted mean of primary patency rate at 12 month at a combination of 55% Post-Thrombotic Syndrome (PTS) subjects at a primary patency rate of 77.1% and 45% non-thrombotic iliac vein lesions (NIVL) subjects at a primary patency rate of 93.4%. The 12-month weighted primary patency rate in the VENOVO® Venous Stent group was 88.3% with 90% CI [82.4%, 94.2%], a statistically significant difference from a literature-derived PG of 74% (one-sided p-value <0.0001).

Table 8: Summary of the Primary Effectiveness Endpoint (ITT Subjects)

	PTS N = 93 n/N(%) [90% CI]	NIVL N = 77 n/N(%) [90% CI]	VENOVO® Unweighted N = 170 n/N(%) [90% CI]	VENOVO® Weighted N = 170 % [90% CI]	p-value
Primary Patency at 12 Months	65/80 (81.3) [72.6,88.1]	63/65 (96.9) [90.6,99.5]	128/145 (88.3) [82.9,92.4]	88.3 [82.4,94.2]	<.0001
	n/N(%)	**n/N(%)**	**n/N(%)**	**%**	
Subjects Failed at 12 Months	15/80 (18.8)	2/65 (3.1)	17/145 (11.7)	11.7	
TVR	11/80 (13.8)	1/65 (1.5)	12/145 (8.3)	8.3	
Thrombus Occlusion	1/80 (1.3)	0	1/145 (0.7)	0.7	
> 50% Stenosis	7/80 (8.8)	1/65 (1.5)	8/145 (5.5)	5.5	

Note: PTS, NIVL and VENOVO® Unweighted 90% CI is estimated by exact binomial method. VENOVO® Weighted is combined patency rate of PTS and NIVL with 55% and 45% weight, respectively, and its 90% CI and one sided p-value is from the weighted Z-statistics and the combined patency rate was tested against the Performance Goal (PG) (74%). A subject may fail due to multiple reasons. The primary effectiveness endpoint was evaluated using the 145 ITT subjects with evaluable 12-month follow-up imaging.

The Kaplan-Meier analysis of primary patency per subject was performed and results are provided in Figure 9. The Kaplan-Meier estimate of primary patency at 12 months (day 395) was 88.9%.

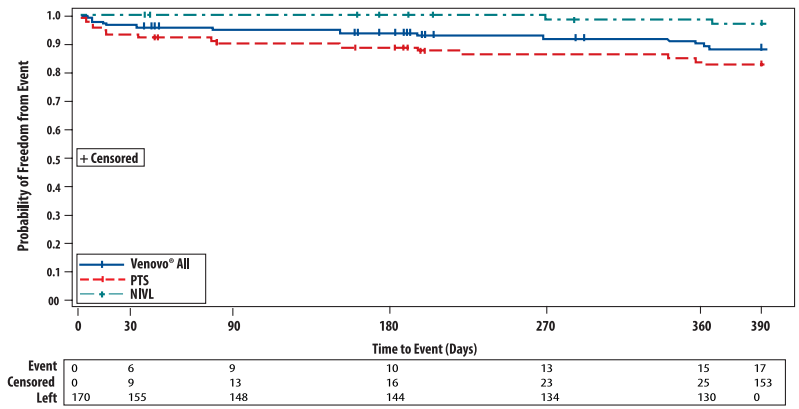


Figure 9: Kaplan-Meier Analysis of Primary Effectiveness Endpoint (ITT Subjects)

Summary of Safety

The primary safety endpoint of the study was freedom from MAEs through 30 days post-index procedure as adjudicated by the CEC. To demonstrate acceptable safety, the primary safety endpoint was evaluated against the PG of 89% which was set at 10% below the literature-derived average freedom from MAE rate at 30 days of 99%. The proportion of subjects free from primary safety events was 93.5% with 90% CI [89.5%, 96.3%], a statistically significant difference from literature-derived PG of 89% (one-sided p-value = 0.0322).

Table 9: Analysis of the Primary Safety Endpoint (ITT Subjects)

Primary Safety Endpoint	PTS N = 93 n/N (%)	NIVL N = 77 n/N (%)	Total N = 170 n/N (%)	90% CI (%)	p-value
Freedom Composite Safety Events (MAE) through 30 Days	82/93 (88.2)	77/77 (100.0)	159/170 (93.5)	[89.5,96.3]	0.0322
Had Failure	11/93 (11.8)	0	11/170 (6.5)		
TVR	6/93 (6.5)	0	6/170 (3.5)		
Pulmonary Embolism (not device or procedure related)	1/93 (1.1)	0	1/170 (0.6)		
Device or procedure-related acute DVT	10/93 (10.8)	0	10/170 (5.9)		

Note: The primary safety endpoint is freedom from major adverse events (MAEs) through 30 days post-index procedure, as adjudicated by CEC. The p-value is computed compared with performance goal = 89% on one-sided exact binomial test. The 90% confidence interval is calculated using the exact binomial method. A subject may fail due to multiple MAEs.

A survival analysis of the primary safety endpoint was also performed. The proportion of subjects free from primary safety events by Kaplan-Meier estimates for 30 days was 93.5%. Refer to Figure 10 for the Kaplan-Meier Analysis.

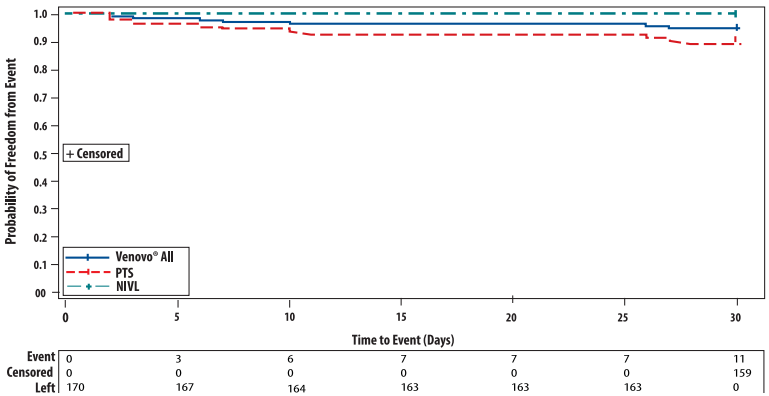


Figure 10: Kaplan-Meier Analysis of the Primary Safety Endpoint (ITT Subjects)

Additional Safety Endpoints

An overview of AEs during the 12-month follow-up period is presented in Table 10. The CEC reviewed all adverse events during the study and it was determined that no serious adverse events (SAEs) were definitely device related.

Table 10: Summary of CEC Adjudicated AEs during the 12-Month Follow-Up Period (ITT Subjects)

	PTS (N=93)		NIVL (N=77)		Venovo® (N=170)	
	By Events	By Subjects	By Events	By Subjects	By Events	By Subjects
Any Adverse Events	75	43(46.2%)	54	31 (40.3)	129	74 (43.5)
Device Relatedness						
Definitely Related	1	1 (1.1%)	0	0	1	1 (0.6)
Possibly Related	31	25 (26.9%)	15	12 (15.6)	46	37 (21.8)
Not Related	43	17 (18.3%)	39	19 (24.7)	82	36 (21.2)
Procedure Relatedness						
Definitely Related	6	6 (6.5%)	9	7 (9.1)	15	13 (7.6)
Possibly Related	39	27 (29.0%)	19	13 (16.9)	58	40 (23.5)
Not Related	30	10 (10.8%)	26	11 (14.3)	56	21 (12.4)
Serious AE (SAE)	46	27 (29.0%)	26	17 (22.1)	72	44 (25.9)
Device Relatedness						
Definitely Related	0	0	0	0	0	0
Possibly Related	16	12 (12.9%)	1	1 (1.3)	17	13 (7.6)
Not Related	30	15 (16.1%)	25	16 (20.8)	55	31 (18.2)
Procedure Relatedness						
Definitely Related	1	1 (1.1%)	2	2 (2.6)	3	3 (1.8)
Possibly Related	19	15 (16.1%)	3	3 (3.9)	22	18 (10.6)
Not Related	26	11 (11.8%)	21	12 (15.6)	47	23 (13.5)

Note: Subjects are only counted once with the highest level of relatedness. Events were coded using MedDRA version 16.1. All AEs up to day 395 were included.

Data regarding device deficiencies and deaths (none of the deaths were related to the device or procedure) were also obtained through 12-month follow-up. There was one (1) reported device deficiency that was not associated with an adverse event and four (4) subjects expired through Day 395. Two deaths were classified as unknown, one (1) myocardial infarction, and one (1) due to cancer. The death events were adjudicated by the CEC and determined to not be related to the study device or procedure.

Summary of Secondary Endpoint Results

Figures 11 and 12 below provide a summary of the secondary effectiveness endpoints at the time of this analysis.

Predetermined secondary endpoints are also presented at 12 months of follow-up. The 12-month Venous Clinical Severity Score (VCSS) change from baseline in the total study population was -1.7 with a 95% confidence interval of -1.81 to -1.49 ($P < .0001$). The 12-month Quality of Life (QoL) assessment of Chronic Venous Insufficiency Questionnaire (CIVIQ-20) score change from baseline in the total study population was -15.7 with a 95% confidence interval of -18.41 to -12.96 ($P < .0001$).

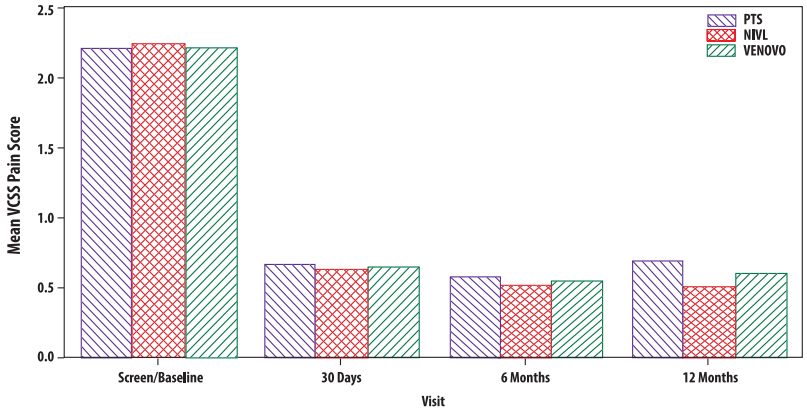


Figure 11: VCSS Pain Score at 12 Months (ITT Subjects)

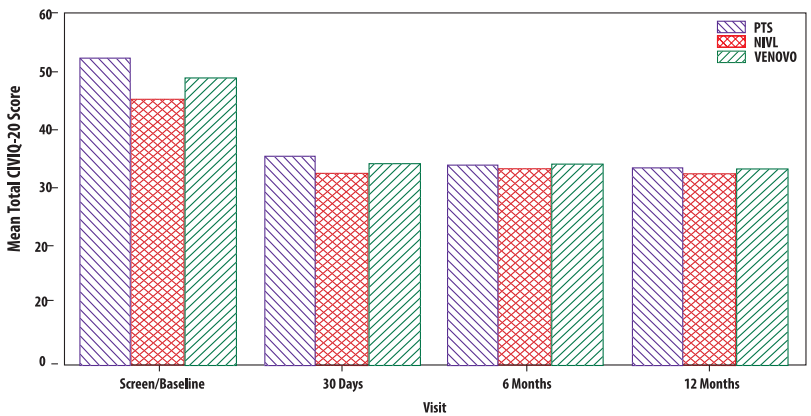


Figure 12: Total CIVIQ-20 Score (ITT Subjects)

Secondary Endpoints without Hypothesis Testing

The following secondary endpoints are limited to descriptive statistics without formal hypothesis testing and are presented here at 12 months of follow-up. One-hundred percent of the Venovo® Venous Stents used in the study were successfully deployed at the intended target with adequate lesion coverage. In addition, 100% of the treated lesions had ≤ 50% residual stenosis post-stent placement and zero stent fractures at the 12-month endpoint.

Table 11: Secondary Endpoints without Hypothesis Testing

	All Subjects N = 170			
	PTS (N = 93) n/N (%)	NIVL N = 77 n/N (%)	Total N = 170 n/N (%)	95% Confidence Interval
Acute Technical Success	93/93 (100.0)	77/77 (100.0)	170/170 (100.0)	[97.9%,100.0]
Acute Procedure Success	91/93 (97.8)	77/77 (100.0)	168/170 (98.8)	[95.8%,99.9]
Lesion Success	93/93 (100.0)	77/77 (100.0)	170/170 (100.0)	[97.9%,100.0]
Freedom from TLR				
30 Day	87/93 (93.5)	77/77 (100.0)	164/170 (96.5)	[92.5%,98.7]
6 Months	84/93 (90.3)	77/77 (100.0)	161/170 (94.7)	[90.2%,97.6]
12 Months	78/89 (87.6)	73/74 (98.6)	151/163 (92.6)	[87.5%,96.1]
Freedom from TVR				
30 Day	87/93 (93.5)	77/77 (100.0)	164/170 (96.5)	[92.5%,98.7]
6 Months	84/93 (90.3)	77/77 (100.0)	161/170 (94.7)	[90.2%,97.6]
12 Months	78/89 (87.6)	73/74 (98.6)	151/163 (92.6)	[87.5%,96.1]
Freedom from Stent Fracture				
12 Months	72/72 (100.0)	65/65 (100.0)	137/137 (100.0)	

Note: 95% confidence interval is estimated by the exact binomial method. A subject may have multiple MAEs. Primary Patency (defined as freedom from TVR; freedom from thrombus occlusion and stenosis > 50% as measured by DUS) at 24 and 36 months will be presented in subsequent clinical study reports.

CONCLUSION

The prospective, multi-center, non-randomized, single-arm study of the Bard Venovo® Venous Stent in the treatment of Iliofemoral Occlusive Disease (VERNACULAR) compared co-primary safety and effectiveness measures to a Performance Goal (PG) derived from published clinical literature to demonstrate the safety and effectiveness of the Venovo® Venous Stent.

Both primary safety and effectiveness endpoint results were demonstrated to have a statistically significant difference from the established PG. Additionally, the Venovo® Venous stent demonstrated excellent deliverability with 100% acute technical success and lesion success with zero stent fractures reported at the 12-month endpoint. Freedom from TLR and TVR at 12 months was 92.6% for both endpoints. Moreover, statistically significant improvements of both the VCSS Pain Score and CIVIQ-20 score, were reported from baseline to 12-months.

The VERNACULAR study results provide scientific evidence that the Venovo® Venous Stent System is safe and effective for the treatment of symptomatic iliofemoral venous outflow obstruction.

Symbols used on Labeling

Consult Instructions For Use

Keep Away From Sunlight

Keep Dry

Do Not Use If Package Is Damaged

Single Use

Do Not Resterilize

Contents: (1)

MR Conditional

Not Made With Natural Rubber Latex

Non-Pyrogenic

Catalogue Number

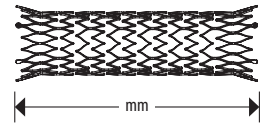
Lot Number

Sterilized Using Ethylene Oxide

Use By

Minimum Introducer Size

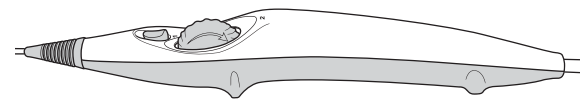
Guidewire Compatibility



Stent Length

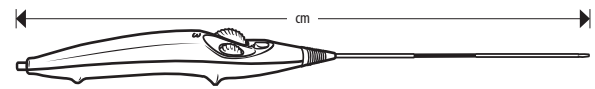
Stent Diameter

Radiopaque Markers



Triaxial Delivery System

Working Length



System Length

Manufacturer

Rx Only

Caution: Federal (USA) law restricts this device to sale by or on the order of a physician

Labeling issue date: 2018-08

VENOVO®

Venous Stent System

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