LimFlow
Transforming CLTI

LimFlow® System

Stent Graft, Infrapopliteal, Venous Arterialization

Instructions For Use

INFORMATION FOR USE

Caution: Federal law (U.S.) restricts the use of this device to sale by or on the order of a physician.

Device Description

The LimFlow® System is comprised of self-expanding conical and cylindrical nitinol stents of varying lengths, covered with an electrospun PTFE covering (BioWeb™), four radiopaque Tantalum markers on the stent graft ends (Figure 1), and is loaded onto a delivery system for deployment (Figure 2). The device is introduced percutaneously through a commercially available sheath into the femoral artery.

The LimFlow System should be used exclusively with the following LimFlow devices when performing the Transcatheter Arterialization of the Deep Veins (TADV) procedure:

- LimFlow Venous Catheter
- LimFlow Arterial Catheter
- LimFlow Valvulotome

The stent is offered in both cylindrical and conical shapes with varying stent lengths and diameters, which are listed in Table 1 where "X" indicates the available stent configuration.

Table 1: Stent Size Matrix

Stent Design	Stent diameter (nominal) [mm]	Working length (nominal) [mm]			
		60	100	150	200
Conical	3.5-5.5	X			
	4.0-5.5	X			
Cylindrical	5.5	X	X	X	X

Conical stents are used to make the arterio-venous connection permanent whereas cylindrical stents are used to extend the stent graft down to the ankle region.

The stent graft system does not contain any hazardous, medicinal, human, or animal materials and substances to which patients would be exposed.

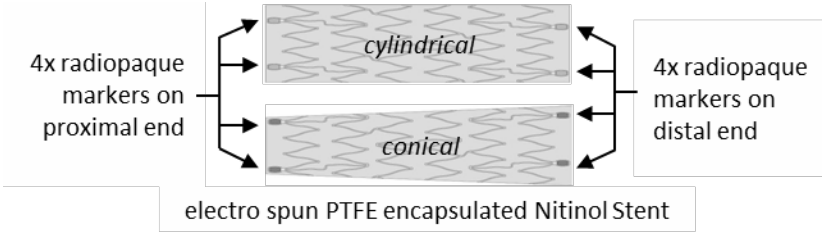

Figure 1: LimFlow Stent Graft Cylindrical (above) and Conical (below)

The stent graft is supplied pre-mounted between the inner catheter and the outer sheath on the distal end of the endovascular system. In this compressed configuration, the Nitinol stent struts lie close together and the radiopaque markers appear as a contiguous band at each end of the stent graft. The stent is deployed using a handle which features a knob that is activated by the user, as shown in Figure 2.

The features of the delivery system are as follows:

- Usable length of the delivery system: 120 cm.
- Crossing profile of delivery device: 7Fr
- 0.018" guidewire compatible
- Radiopaque markers located at the device tip; proximal and distal stent pocket markers; and four markers on each end of stent graft

Handle mechanism: The proximal side of the Handle delivery system consists of a knob that translates rearward during deployment moving with it a carriage assembly by means of a gear and rack mechanism which retracts the outer sheath while the inner tubing is stationary. During delivery of the implant to the target site, unintended stent movement is restricted by the safety clip which locks the carriage in place until the physician is prepared to deploy. During the deployment forward (distal) motion of the sheath is prevented by means of a pawl and ratchet mechanism which only permits further rearward motion of the carriage and outer sheath once deployment has been initiated. The handle also features a strain relief at the distal end to allow for a kink-resistant transition between the rigid handle and flexible shaft assembly when the device is tracked in the patient. The distal aspect consists of the outer tubing, containing the loaded stent graft, and the inner catheter which includes the guidewire lumen, distal and proximal radiopaque markers, and atraumatic distal tip. Coaxial to the guidewire lumen is the midlayer, which serves to permit stent deployment as the outer tubing is retracted.. The two ports on the handle help facilitate flushing of the guidewire and stent graft lumens prior to the procedure.

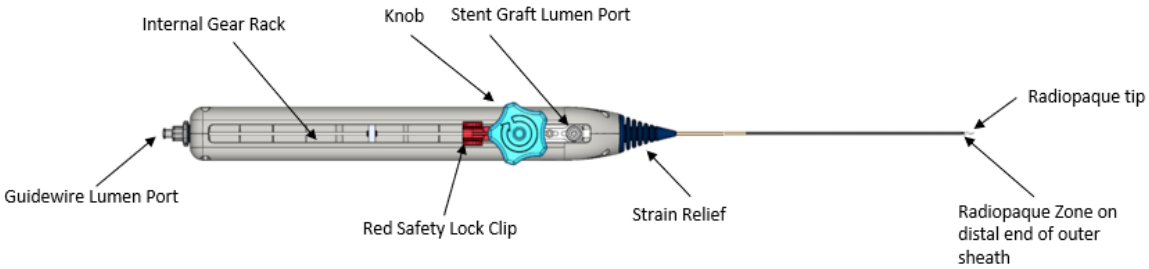

Figure 2: LimFlow Handle Delivery System

How Supplied:

The LimFlow System is supplied sterile (by ethylene oxide gas). For single use only.

Indications for Use:

The LimFlow System is indicated for patients who have chronic limb-threatening ischemia with no suitable endovascular or surgical revascularization options and are at risk of major amputation.

Contraindications:

The LimFlow System is contraindicated in the following patient populations:

- Patients with deep venous thrombus in target vein.
- Patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy.

Warnings:

- The use of the device should be limited to those specialists trained to perform the procedures for which this device is intended.
- The device should not be used without first reading and understanding these directions in their entirety.
- The LimFlow System is designed and intended for single use only. Do not autoclave, reshape, re-sterilize or reuse. Exposure to high heat may cause changes to the functionality of the device. Reuse, even if re-sterilized, can compromise the LimFlow System performance characteristics and may cause infection.
- Do not use organic solvents (e.g., alcohol) with the delivery system.
- Use in patients with concomitant hepatic insufficiency has not been evaluated.
- Use in patients with poor cardiac output, e.g., NYHA Class IV, has not been evaluated.
- Use in pregnant and breastfeeding women has not been evaluated.

Precautions:

- Do not use if packaging has been previously opened or damaged.
- Use the LimFlow System prior to expiration date specified on the package.
- Inspect the LimFlow System prior to use to verify the size and condition as being suitable for the specific procedure.

- Always protect the LimFlow delivery system and its tip from impact and excessive force. Do not attempt to reshape the delivery system tip, since reshaping may damage internal components of the device.
- Implanting the device in the distal half of the calcaneus may result in stent fracture.
- Store at room temperature in a dark dry place. Do not expose catheter to strong solvents.
- Advancement, manipulation, and withdrawal of the LimFlow System should always be performed under fluoroscopic guidance. If substantial resistance is met during manipulation, immediately discontinue the procedure and determine the cause of the resistance before proceeding. If the cause of the resistance cannot be determined, withdraw the LimFlow System.

Potential Complications:
Complications and Adverse Events associated with the use of the LimFlow System may include the usual complications associated with endovascular stent and stent graft placement and dialysis shunt revisions.

Potential complications that may possibly be caused by or associated with the use of the device or the related procedures, and which may or may not require endovascular or surgical treatment include:

- Acute renal impairment requiring dialysis
- Anesthesia reactions including respiratory difficulties, sedation induced apnea, pneumonia, low blood
- Cardiac arrest
- Death
- Embolization
- Gas embolism from procedural error or equipment malfunction with embolic phenomenon
- Graft rupture, trans-graft leak, site leak
- Hematoma
- Heparin reactions including bleeding, thrombosis, changes in circulating blood elements and skin necrosis
- Insufficient blood flow to foot
- Ionic and non-ionic radiopaque contrast medium, major complications: life- threatening reactions including cardiovascular collapse, severe respiratory difficulty, nervous system dysfunction, convulsions, coma, and cardio-respiratory arrest
- Ionic and non-ionic radiopaque contrast medium, minor complications: allergic reactions including nausea, vomiting, facial flush, feeling of body warmth, dermal manifestations of urticaria with or without pruritus, erythema and maculopapular rash, dry mouth, allergic glossitis, sweating, conjunctival, symptoms, facial, peripheral, and angio-neurotic edema
- Ischemia
- Medication side effects, drug reaction
- Myocardial infarction
- Occlusion
- Pain
- Peripheral edema
- Procedural bleeding
- Restenosis of stented segment
- Sepsis / Infection
- Stent damage, implant migration
- Stent graft fracture
- Stent graft misplacement, deformation, or migration
- The need for surgical or endovascular interventions to rectify an access site problem
- Thrombosis
- Vessel dissection, perforation, injury
- Vessel spasm

MRI Safety Information  MR Conditional	Non-clinical testing, MRI simulations, and human body model for *in vivo* modeling demonstrated that every version of the LimFlow System is MR Conditional. A patient with the LimFlow System may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.
Parameter	Condition
Nominal Values of Static Magnetic Field (T)	1.5-T or 3.0-T
Maximum Spatial Field Gradient (T/m and gauss/cm)	30-T/m (3,000-gauss/cm)
Type of RF Excitation	Circularly Polarized (CP) / Quadrature-transmission
Transmit RF Coil Information	There are no transmit RF coil restrictions. Accordingly, the following may be used: body transmit RF coil and all other RF coil combinations (i.e., body RF coil combined with any receive-only RF coil, transmit/receive head RF coil, transmit/receive knee RF coil, etc.)
Operating Mode of MR System	Normal operating mode with the following whole-body averaged: • For an imaging landmark above the patient's groin, the maximum acceptable whole-body averaged SAR is 2 W/kg. • For an imaging landmark below the patient's groin, the maximum whole-body averaged SAR is 0.75 W/kg.
Limits on Scan Duration	• For an imaging landmark above patient's groin, a patient can be scanned continuously for 60 minutes. • For an imaging landmark below patient's groin, a patient can be scanned continuously for 30 minutes, with a rest period of 30 minutes or more. The MRI pulse sequence can be repeated
MR Image Artifact	The presence of this implant produces an imaging artifact. Carefully select pulse sequence parameters if the implant is located in the area of interest.

Storage:
Store in a cool, dry, and dark place. Use by the "Use By" date specified on the label.

Disposal Instructions:
After use, this product may be a potential biohazard. Handle and dispose of in accordance with the accepted medical practice and applicable local, state, and federal laws and regulations.

DIRECTIONS FOR USE COMMON TO BOTH DELIVERY SYSTEMS

Prior to use of the LimFlow®System, the TADV procedure should be initiated using other LimFlow devices. The crossing from artery to vein should be accomplished using the LimFlow ARC® arterial catheter and LimFlow V-CEIVER® venous catheter while valvulotomy should be performed using the LimFlow VECTOR® valvulotome. Reference the respective Instructions for Use for additional information. When extending LimFlow stent grafts to the ankle region to enable blood flow to the lower limb, use cylindrical stent grafts. Use the appropriate stent graft lengths to achieve complete coverage from the ankle region to the crossing point. The choice of conical stent used for crossing should be based on patient anatomy and physician discretion. The recommended minimum overlap between stent grafts is 1 cm. Caution: Do not place stents in high flex regions of the leg and foot as this could lead to stent damage. Note: Physician experience and discretion will determine the appropriate drug regimen for each patient.

Accessories required for the implantation:

- Introducer sheath of appropriate size (7Fr or larger)
- 0.018" diameter guidewire (exchange length, 300 cm)
- Syringe with Luer lock for flushing
- Sterile, heparinized saline solution
- Appropriate catheters and accessories
- Contrast medium
- PTA balloons

Pre-Deployment Procedure:

- Inject Contrast Media & Sizing
    - Perform diagnostic angiography using standard technique to confirm site of implantation and determine appropriate stent size. Proper stent sizing is critical for correct positioning and to avoid stent migration.
    - To ensure adequate anchoring, the diameter of the stent graft should be approximately 0.5mm larger than the vessel diameter.
- Evaluate and Mark Target Site
    - Fluoroscopically evaluate and mark the target site

LimFlow System Sizing and Selection:

Special care must be taken to ensure that the appropriate LimFlow System is selected prior to introduction. Proper sizing is critical for correct positioning and to avoid stent migration. To ensure adequate anchoring, the diameter of the stent graft should be approximately 0.5mm larger than the vessel diameter.

Table 2: LimFlow System Sizing and Selection Table

Stent Graft Size	Stent Part Number	Stent Graft Length [mm]	Stent Graft diameter [mm]		Recommended vessel diameter [mm]	
			Proximal	Distal	Proximal	Distal
3.5 mm Conical Stent	SGH-35060-US-21	60	3.5	5.5	2.7 – 3.0	4.5 – 5.0
4.0 mm Conical Stent	SGH-40060-US-21	60	4.0	5.5	3.0 – 3.5	4.5 – 5.0
60 mm Cylindrical Stent	SGH-55060-US-21	60	5.5	5.5	4.5 – 5.0	
100 mm Cylindrical Stent	SGH-55100-US-21	100	5.5	5.5	4.5 – 5.0	
150 mm Cylindrical Stent	SGH-55150-US-21	150	5.5	5.5	4.5 – 5.0	
200 mm Cylindrical Stent	SGH-55200-US-21	200	5.5	5.5	4.5 – 5.0	

Note: The foreshortening on all stent grafts is less than 5%

DIRECTIONS FOR USE – HANDLE DELIVERY SYSTEM

Preparation:

1. Open the box and remove the pouch containing the stent system.
2. Carefully inspect the pouch for damage to the sterile barrier. Then, peel the pouch open and remove the packaging card containing the stent system. Extract the stent system from the packaging card by opening the clips and check the following:
    - Verify that the red safety lock (Figure 3) is still securely in place.
    - Examine the stent system for any damage. If it is suspected that the sterility or performance of the device has been compromised, the device should 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.
3. Flush both lumen of the device with heparinized saline prior to use. The stent graft lumen port is distal to the knob and the guidewire lumen port is on the proximal end of the unit (Figure 4).

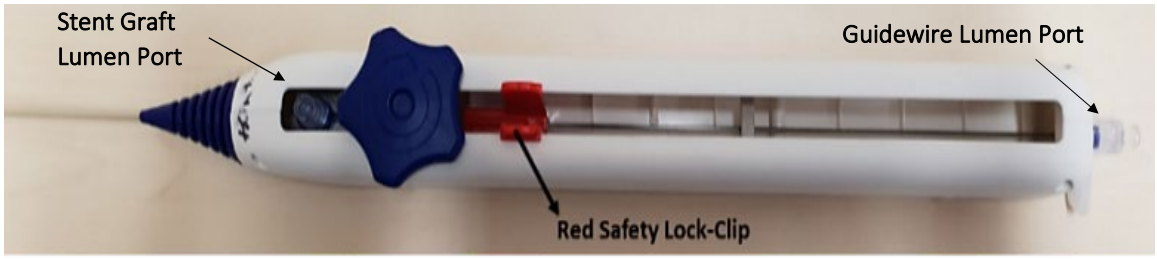

Figure 3: Red Safety Lock and Flushing Ports

4. Caution: After flushing the guidewire lumen and removing the syringe, ensure that the clear luer is locked securely to the blue luer of the handle by turning the clear luer tightly in the clockwise direction.

Figure 4: Luer connection at the proximal end of the handle

5. Wipe the usable length portion of the stent system with saline-soaked gauze.

Insert Introducer Sheath and Guidewire

1. Gain access at the appropriate site utilizing a 7Fr (or larger) introducer sheath.
2. Insert a guidewire of appropriate length and diameter (maximum 0.018") across the arterio-venous connection created by the LimFlow Arterial and Venous catheters to be stented via the introducer sheath.

Dilate Stricture

1. If the physician deems that pre-dilatation is required, standard techniques (e.g. PTA balloon catheter) may be used. While maintaining site access with a guidewire, remove the PTA balloon catheter from the patient.

Introduce the LimFlow System

1. Advance the device over the guidewire through the sheath introducer. Note: If resistance is met during stent system introduction, the system should be withdrawn and another system should be used. Caution: Always use an introducer sheath for the implant procedure to protect the vasculature and the puncture site.
2. Position the distal marker of the delivery system past the target site.
3. Ensure the delivery system is pinned to a flat surface and is as straight as possible out of the femoral sheath. Caution: Any slack in the stent system (outside the patient) could result in deployment challenges.

Deploy Stent

1. Verify that the stent end is distal to the target site.
2. Confirm that the introducer sheath is secure and will not move during deployment. Caution: Ensure once again the security of the proximal luer lock.
3. Remove the red safety clip immediately prior to deployment (Figure 5) by pinching the tabs together and pulling the clip straight out of the unit.
4. Verify the position of the device using fluoroscopy.

5. Initiate deployment by slowly turning the blue knob in a clockwise fashion while maintaining back tension on the handle. The knob will translate rearward with deployment (Figure 6). The knob should not be rotated in a counterclockwise fashion at any stage during the deployment process. Note that the implant cannot be re-captured once deployment has been initiated. Be sure to avoid interaction with the retracting outer sheath as doing so could prevent deployment.
6. After the first 15mm have been deployed wait for the stent graft to open and engage the vessel wall prior to continuing.
7. Verify the completion of deployment and final position of the device using fluoroscopy.

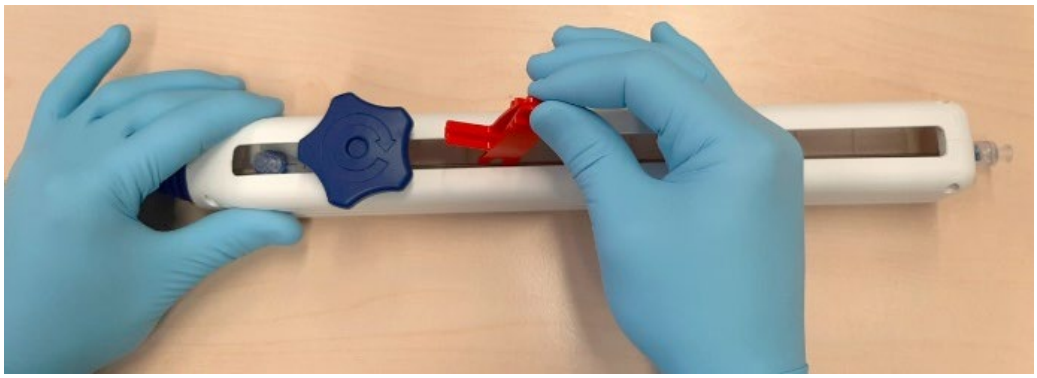

Figure 5: Removal of the red safety clip

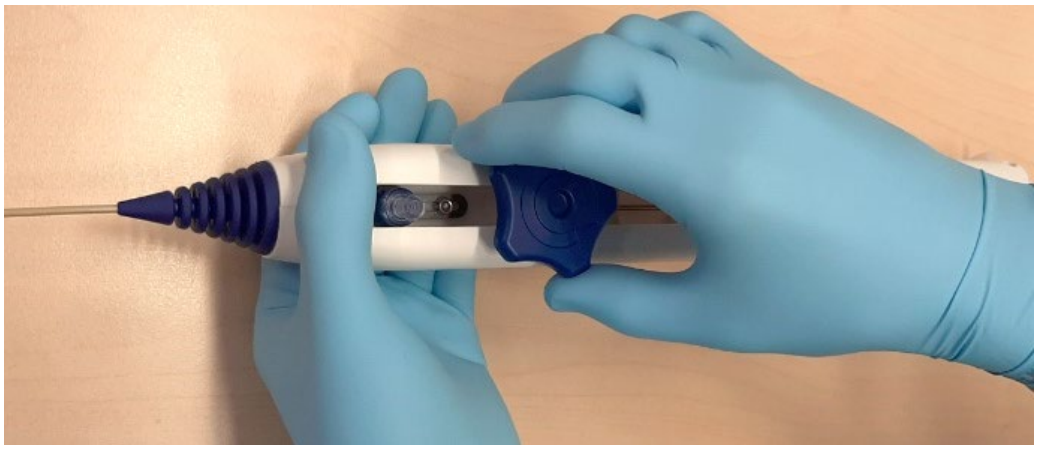

Figure 6: Correct deployment using the handle

Post Stent Placement

1. Remove the delivery device from the body. Note: The catheter's tip can be retracted to the extrusion after unlocking the clear luer at the handle's end (refer to Figure 5). Pull the clear luer and lock the metal using the white clamp before retracting the delivery device from the body (if desired).
2. Deploy additional stents as needed to create the percutaneous deep vein arterialization circuit.
3. If additional stent-to-vessel apposition is desired, select a balloon catheter that matches the size of the reference vessel and chosen stent graft size but not larger than the stent diameter itself.
    - Conical stent post-dilation: Recommended balloon size: ø4 mm
    - Cylindrical stent post-dilation: Recommended balloon size: ø5 mm
4. At the physician's discretion, inflow and outflow procedures (including use of the LimFlow valvulotome) may be performed in the lower foot to optimize blood flow and make the vein valves incompetent. See the LimFlow valvulotome Instructions for Use.
5. Remove the guidewire and introducer sheath from the body.
6. Close entry wound as appropriate.
7. Discard the delivery device, guidewire, and introducer sheath.

PATIENT IMPLANT INFORMATION CARD

A Patient Implant Information Card is provided with this device. The Patient Data, Implant Data, and Hospital Data should be carefully recorded on the card and given to the patient. Apply one of the peel-off stickers found on the product labels on the product carton box or on the pouch to the indicated area on the Patient Implant Information card. This peel-off sticker contains important information about the patient's stent graft implant. The patient should carry this card with them and provide to any medical personnel caring for the patient in the future.

SUMMARY OF CLINICAL STUDY

A clinical study PROMISE II (NCT03970538) was performed to establish a reasonable assurance of safety and effectiveness of the LimFlow System using the Transcatheter Arterialization of the Deep Veins (TADV) procedure for treating no-option patients with chronic limb-threatening ischemia (CLTI) by creating an arteriovenous connection in the below-the-knee vasculature in the United States. The primary safety and effectiveness endpoint was Amputation-Free Survival (AFS), which was defined as freedom from major (above ankle) amputation and death, at six months compared to a historical performance goal. The population included in determination of the PROMISE II Trial primary endpoint was all members of the Modified Intent-To-Treat Population (mITT) available for follow-up at the 6-month time point. The mITT population was defined as all subjects where a LimFlow device was introduced into the patient, regardless of technical or procedural success or major protocol deviation. The LimFlow System is comprised of Arterial and Venous (AV) Crossing Catheters, Valvulotome, and LimFlow self-expanding crossing and extension stent grafts.

A. Study Design

The PROMISE II Study was a prospective, single-arm, multi-center pivotal study conducted in the United States designed to confirm the safety and effectiveness of the LimFlow System in a no-option CLTI population. The study was designed to consist of a minimum of 60 and up to 120 subjects. This study utilized a Bayesian Goldilocks adaptive design for sample size determination. Following a series of interim analyses, a total of 105 subjects were enrolled. The subjects were reviewed by an independent committee of vascular surgeons to determine eligibility based on a) absence of a usable pedal artery target (endovascular or surgical approach), or b) the presence of a pedal artery target with absence of a viable single-segment vein in either lower extremity or either arm that could be used for autogenous vein conduit. Wound photography was assessed by an independent wound core lab at all follow-up visits, and patency (via duplex ultrasound) was assessed by an independent imaging core lab at 1-month and 6-months. An independent Clinical Events Committee (CEC) reviewed and adjudicated any endpoint events such as amputations, renal sequelae, re-interventions, stent occlusions, and subject deaths. A Data Monitoring Committee (DMC) acted in an advisory capacity to the Sponsor in the monitoring of participant safety and evaluation of the progress of the study.

This was evaluated using a Bayesian method in which the six-month AFS rate was assigned a uniform prior distribution and mathematically updated after observing binary six-month outcomes; subjects with incomplete follow-up were included in the final analysis via Bayesian multiple imputation. By design, subjects without death or major amputation who had incomplete follow-up had their unknown final outcome repeatedly imputed with subject-specific probabilities of having an event dependent on the subject's amount of event-free follow-up time. The imputation model followed a Bayesian piecewise exponential survival model fitted to the full dataset for all subjects; results of the many "filled-in" or "completed" datasets were then combined into a single posterior probability of success.

The criterion of trial success was a posterior probability of at least 0.977 that the true six-month AFS exceeds an objective performance goal of 54.0%. The threshold of 0.977 was pre-specified to control the study's false positive rate at the level 0.025, as demonstrated in extensive pre-trial simulations. The primary endpoint was analyzed using the methods described above. All secondary endpoint analyses were conducted using frequentist methods and descriptive statistics.

All patients were scheduled to return for follow-up examinations at the following timepoints post-procedure: 2-weeks, 1-month, 3-months, 6-months, 9-months, 12-months, 24-months, and 36-months. An additional visit for duplex ultrasound only was performed at 2-months post-procedure. Adverse events and complications were recorded at all visits.

B. Clinical Endpoints

1. Primary Endpoint
   The primary safety and effectiveness endpoint was Amputation-Free Survival (AFS) defined as freedom from major (above ankle) amputation and death at 6 months compared to a historical performance goal.

   Subgroup analysis of the primary endpoint was included in the study with the following pre-specified sub-groups:
   - Sex (Male/Female)
   - Dialysis status (Yes/No)
   - Age (≤ 70, > 70)
   - Diabetes (Type I/Type II, None)
   - Race/Ethnicity
   - Rutherford Classification

2. Secondary Endpoints
   The secondary endpoints in this study included Primary Patency, Primary Assisted Patency, Secondary Patency, Limb Salvage, Change in Rutherford Classification, Technical Success, Procedural Success, Target Wound Healing, All Wound Healing, All Wound Area Reduction, Freedom from Contrast-Induced Nephropath, Procedure Time, Radiation Exposure, and Contrast Volume.

C. Demographics and Baseline Parameters

The demographics of the study population are typical for a study performed on CLTI patients. The study population's baseline key demographics and medical history are reported in Table 3 and Table 4 for all 105 subjects.

Table 3: Baseline Demographics

	N=105
Age, years (SD)	69.0 (10.4)
Sex, male	68.6% (72/105)
Race	
Asian	1.9% (2/105)
Black or African descent	15.2% (16/105)
Caucasian	61.0% (64/105)
Declined to state	21.9% (23/105)
Ethnicity	
Hispanic or Latino	27.6% (29/105)
Not Hispanic or Latino	72.4% (76/105)
BMI (SD)	26.2 (5.32) (N=104[1])
Smoking history (current or past smoker)	41.9% (44/105)
Past smoker, not current	36.2% (38/105)
Current smoker	5.7% (6/105)
Never smoked	58.1% (61/105)

[1]BMI information for one subject was not available.

Table 4: Medical History

Characteristic	N=105
Diabetes	77.1% (81/105)
Type I	13.6% (11/81)
Type II	86.4% (70/81)
Chronic Kidney Disease (CKD)	39.0% (41/105)
Dialysis	18.1% (19/105)
Autologous arteriovenous fistula	63.2% (12/19)
Peritoneal dialysis	36.8% (7/19)
Hypertension	91.4% (96/105)
Hyperlipidemia	69.5% (73/105)
Prior MI	22.9% (24/105)

Prior stroke	8.6% (9/105)
Hepatic insufficiency	3.8% (4/105)
Prior deep vein thrombosis	3.8% (4/105)
Heart Failure	20.0% (21/105)
Prior intervention to target limb	74.3% (78/105)
Baseline Rutherford Class 6	35.2% (37/105)
Baseline Rutherford Class 5	64.8% (68/105)

D. Subject Accountability

At the time of database lock, 105 patients were enrolled in the PMA study. One subject did not receive the device, and four subjects withdrew or were lost-to-follow-up before the 6- month post-operative visit. The patient disposition for the PROMISE II study is provided in Figure 7. The population included in determination of the PROMISE II Trial primary endpoint was all members of the Modified Intent-To-Treat Population (mITT) available for follow-up at the 6-month time point. The mITT population was defined as all subjects where a LimFlow device was introduced into the patient, regardless of technical or procedural success or major protocol deviation. Study subjects will remain in this study through 3-year follow-up unless they exited either (a) prematurely due to withdrawal of consent to continue or (b) at the point they reached the primary study endpoint of AFS (either major above-ankle amputation or death). It should be noted that, post-primary analysis, a subject was found to have expired after study withdrawal by an investigator but prior to completion of 30-day follow-up.

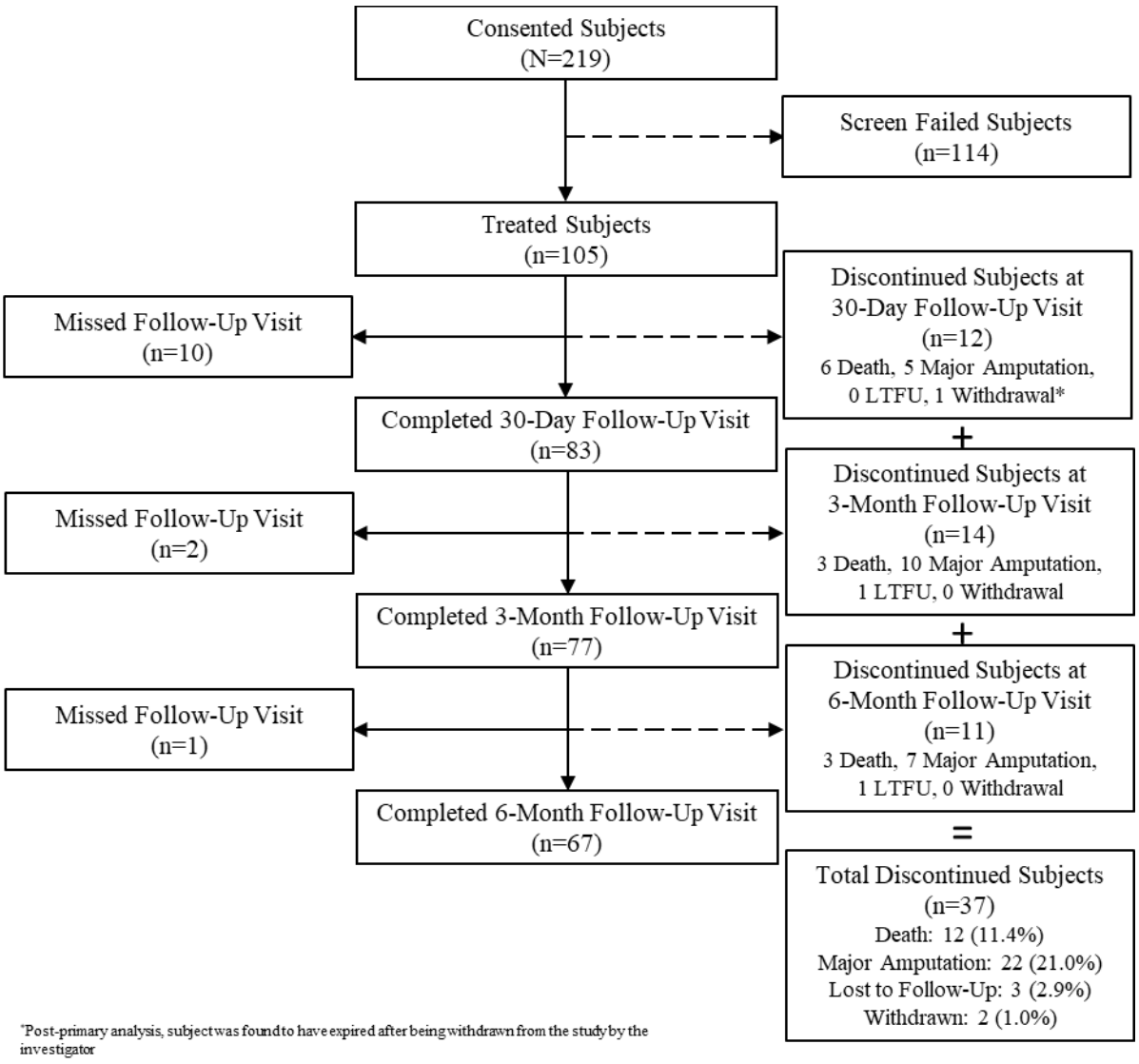

Figure 7: PROMISE II Subject Accountability

E. Safety and Effectiveness Results

1. Procedural Outcomes

Technical success, defined as successful creation of an arteriovenous fistula in the desired limb location with immediate morphological success was achieved in 104 cases resulting in a 99.0% technical success rate. There was one case of technical failure in 105 treated subjects, which occurred when venous arch wiring was not possible, therefore valvulotomy and stenting did not occur.

Procedural success was defined as a composite endpoint accounting for a combination of technical success as well as an absence of all-cause death, above-ankle amputation, or clinically-driven major reintervention of the stent graft through 30 days. As procedural success considers follow-up through 30 days, any subject who exited the study for non-endpoint purposes was excluded from the analysis. Procedural success was achieved in 76.9% of the 104 subjects available for follow-up or who reached the procedure failure endpoint prior to 30 days. The key procedural characteristics are provided in Table 5.

Table 5: Key Performance and Procedure Data

Characteristic	N=105
Technical Success[1]	104/105 (99.0%)
30-day Procedural Success[2]	80/104 (76.9%)
Procedure time, mean (range)[3]	217.1 minutes (84.0 – 576.0)
Total radiation exposure, mean (range)	267.0 milligray (10.2 – 1615.0)
Contrast volume, mean (range)	137.7 mL (5.0 – 490.0)

[1] Technical Success was defined as: percentage of subjects with completion of the endovascular procedure and immediate morphological success.

[2] Procedural Success was defined as: percentage of subjects with combination of technical success, and absence of all-cause death, above-ankle amputation or clinically driven major re-intervention of the stent graft at 30 days.

[3] Defined as successful arterial or venous puncture (whichever was done first) to removal of last catheter

2. Safety Results

The analysis of safety was based on the mITT cohort of 105 patients available for the 6-month evaluation. The key safety outcomes for this study are presented in Table 6.

Table 6: Key Safety Results

Characteristic[1]	
30-day Mortality[2]	6/99 (6.1%)
6-month Mortality[2]	12/80 (15.0%)
30-day Major Amputation (Below-knee)	5/98 (5.1%)
3-month Major Amputation (Below-knee)	15/94 (16.0%)
6-month Major Amputation (Below-knee)	23/91 (25.3%)
Freedom from contrast-induced nephropathy through 72 hours post-procedure	103/105 (98.1%)

[1]All denominators represent the subjects available for follow-up to that time point plus any subject who experienced that event prior to a premature exit, where applicable.

[2]One additional subject was found to have expired after being withdrawn from the study by an investigator 5 days following the study procedure. The Post-Hoc analysis in Table 14 accounts for this patient death.

3. Adverse effects that occurred in the clinical study

All study adverse events (AE) were reported by sites for Seriousness and then processed by MedDRA coding with System Organ Class (SOC) and Preferred Term (PT) by a medical monitor. They were evaluated further for unanticipated adverse device effect (UADE) status by the medical monitor.

Device- and procedure-relatedness was assessed by the study CEC for any events that required adjudication (study endpoint-qualifying events). All adverse events occurring within 30 days of the procedure were, by CEC charter definition, considered procedure-related during adjudication and are listed in Table 7. There were no events labelled by the independent medical monitor as unanticipated adverse device effects in the study. As CLTI patients typically have many comorbidities and unrelated adverse events, serious adverse events listed in the following two tables are focused on site-reported adverse events within 30 days post-procedure and serious adverse events through 6 months.

Table 7: Site-reported Adverse Events through 30 days

Event Type	All events	
	During Procedure N=105	Post-Procedure N=105
Amputation of the index limb (major)[1]	0/105 (0.0%)	6/105 (5.7%)
Arterial or venous occlusion[2]	0/105 (0.0%)	2/105 (1.9%)
Arterial/Venous thrombus formation	0/105 (0.0%)	3/105 (2.9%)
Access site bleeding or hematoma requiring reintervention	0/105 (0.0%)	0/105 (0.0%)
Congestive cardiac failure	0/105 (0.0%)	1/105 (1.0%)
Contrast-induced nephropathy and renal failure	0/105 (0.0%)	2/105 (1.9%)
Death[3]	0/105 (0.0%)	6/105 (5.7%)
Infection (local)	0/105 (0.0%)	11/105 (10.5%)
Infection (systemic, sepsis)[4]	0/105 (0.0%)	3/105 (2.9%)
Lower extremity ischemia	0/105 (0.0%)	5/105 (4.8%)
Pseudoaneurysm	0/105 (0.0%)	1/105 (1.0%)
Target limb or wound pain requiring intervention	0/105 (0.0%)	17/105 (16.2%)
Other[5]	3/105 (2.9%)	35/105 (33.3%)

[1] Major amputation is defined as above-ankle amputation of the index limb.
[2] Complete absence of flow on color Doppler, or absence of sound and/or waveform by bedside doppler, and/or absence of flow on angiographic images (conventional or CT)
[3] Post-primary analysis, a subject was found to have expired after withdrawn from the study by the investigator; including this event changes the death rate to 7/105 (6.7%).
[4] Post-primary analysis, an additional case of sepsis was documented. Including this event changes the sepsis rate to 4/105 (3.8%).
[5] Other refer to single events such as headache, anxiety, or vomiting.

There were no device-related events that occurred during the index procedure. CEC-adjudicated device-related adverse events over time are presented in Table 8 with data presented as cumulative incidence of events over time. Due to the nature of reinterventions occurring multiple times in one subject, the total count of events is also presented. All events were adjudicated conservatively as device-related if the device involvement could not be ruled-out. Any occlusion that extended to the area of stenting – regardless of the origin of occlusion – was automatically adjudicated as device-related. Similarly, any reintervention performed which touched a LimFlow stented area of vessel was also adjudicated as device-related.

Table 8: Device and Procedure-Related Site-reported Adverse Events through 6-months[1]

Device-Related Event	30 days	3 month	6 month
Subjects through timepoint	104	103	102
Death (number / device related)	6/0	9/0	12/0
Major Amputation (rate)[2]	3/104 (2.9%)	7/103 (6.8%)	9/102 (8.8%)
Site-reported occlusion or reintervention (occlusive or non-occlusive)			
Count of events[4]	21	46	63
Patients with any event (rate)	18/104 (17.3%)	35/103 (34.0%)	44/102 (43.1%)
Occlusion (no intervention)			
Count of events[4]	1	3	6
Patients with event (rate)	1/104 (0.1%)	2/103 (1.9%)	6/102 (5.9%)
Reintervention of the stent graft			
Count of occlusive events[4]	14	29	39
Count of non-occlusive events[4]	6	14	18
Patients with any reintervention (rate)	18/104 (17.3%)	33/103 (32.0%)	41/102 (40.2%)
Procedure-Related Event[3]			
Death (number / procedure related)	6/6	--	--
Major Amputation (rate)	5/104 (4.8%)	--	--
Contrast-Induced Nephropathy	2/104 (1.9%)	--	--

[1] Denominator includes all patients not lost to follow-up or withdrawn.

[2] Major amputation is defined as above-ankle amputation of the index limb.

[3] Per the Safety Charter, if events were deemed to be device-related, it superseded procedure-relatedness, and no further adjudication was completed for procedure-relatedness. If, however, the event was deemed as unrelated to the study device, procedure-relatedness was adjudicated. All adjudicated adverse events occurring within 30 days of the procedure were by default, procedure-related

[4] Note: Count of events includes all events, even if multiple events occurred in the same patient

The rates of adverse events seen in the study are in line with expectations for this high-risk population which has many comorbidities, and events align with the underlying baseline risk factors and medical history for this population. Investigators were allowed to report clinical experiences associated with standard wound care even if the protocol did not require reporting. Serious adverse events that occurred in >5% of patients are presented in Table 9.

Table 9: Subjects with Serious Adverse Events through 6 months[1]

Serious Adverse Events	n/N (%) where N=105
Death[2]	12/105 (11.4%)
Gastrointestinal hemorrhage	5/105 (4.8%)
Incision site impaired healing	6/105 (5.7%)
Gangrene	10/105 (9.5%)
Osteomyelitis	7/105 (6.7%)
Sepsis[3]	6/105 (5.7%)
Wound infection	6/105 (5.7%)
Wound complication	6/105 (5.7%)
Pain in extremity	6/105 (5.7%)
Acute kidney injury	5/105 (4.8%)
Debridement	5/105 (4.8%)
Peripheral ischemia	6/105 (5.7%)

[1] The events listed in this table are site reported then coded using MedDRA version 21.0 and then stratified by System-Organ Class (SOC) and Preferred Term.

[2] Post-primary analysis, a subject was found to have expired after withdrawal from the study by the investigator; including this event changes the death rate to 13/105 (12.4%).

[3] Post-primary analysis, an additional case of sepsis was documented; including this event changes thesepsis rate to 7/105 (6.7%).

Standard wound care for this patient population includes debridement, negative pressure therapy, and minor amputations. Table 10 provides an overview of all ipsilateral minor and major amputations observed through 6 months.

Table 10: Subjects with Ipsilateral Amputations through 6 months

Ipsilateral Amputation	n/N
Any Ipsilateral Amputation[a]	72/105 (68.6%)
Toe amputation	31/105 (29.5%)
Foot amputation (below ankle, above toe)	42/105 (40.0%)
Major Amputation (below knee)	23/105 (21.9%)

[a] Subjects who had more than one amputation (e.g., toe amputation followed by TMA) are represented in the individual types of amputation but are only counted once in the Any Ipsilateral Amputation rate.

4. Effectiveness Results

The primary analysis of safety and effectiveness was based on the mITT cohort of 105 patients available for the 6-month evaluation as a Bayesian analysis of the 6-month amputation-free survival rate. Multiple imputations were performed to address missing data at the 6-month time point. Kaplan-Meier analyses were also conducted for key effectiveness outcomes of amputation free survival (AFS) and the components (limb salvage and survival) as presented in Figures 8-10 and Tables 11-13. Follow-up beyond 6-months (180 days) is ongoing.

Of the 105 mITT subjects in this analysis, 35 subjects had AFS events and 67 were event-free at 180 days. Three (3) subjects had incomplete follow-up (5 days, 72 days, 100 days) without events; these subjects were censored at these times for the Bayesian piecewise exponential survival model used for multiple imputation.

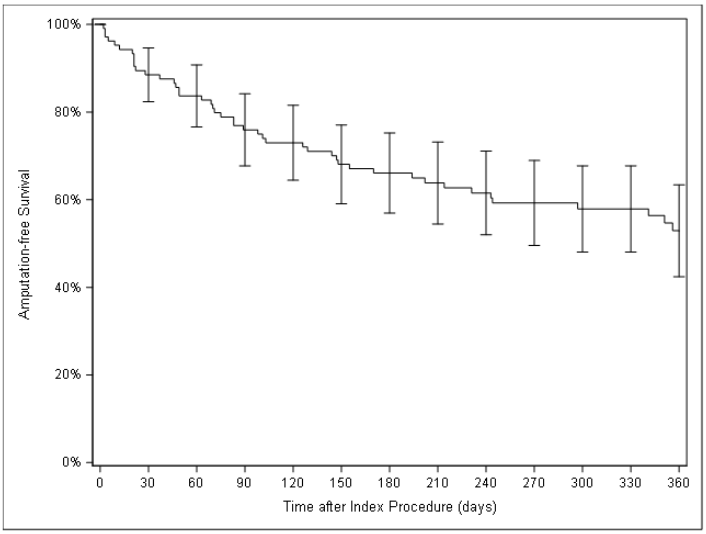

Figure 8: Kaplan Meier Analysis of Amputation-Free Survival (AFS)

Table 11: Analysis of Amputation Free Survival Status over Time

From day X To day Y LimFlow System (N= 105 Subjects)	0 0	1 30	31 60	61 90	91 120	121 150	151 180
# Subjects at Risk	105	105	92	87	78	74	69
# Censored Subjects (Withdrawn or LTFU)	0	1	0	1	1	0	0
# Subjects with Event (Deaths or Major Amputations)	0	12	5	8	3	5	2
Event-free Rate [%]	100.0%	88.5%	83.7%	75.7%	72.5%	67.6%	63.7%
95% Confidence Interval [%]	N/A	80.6% - 93.3%	75.1% - 89.5%	66.5% - 83.1%	63.3% - 80.5%	58.1% - 76.1%	56.1% - 74.3%

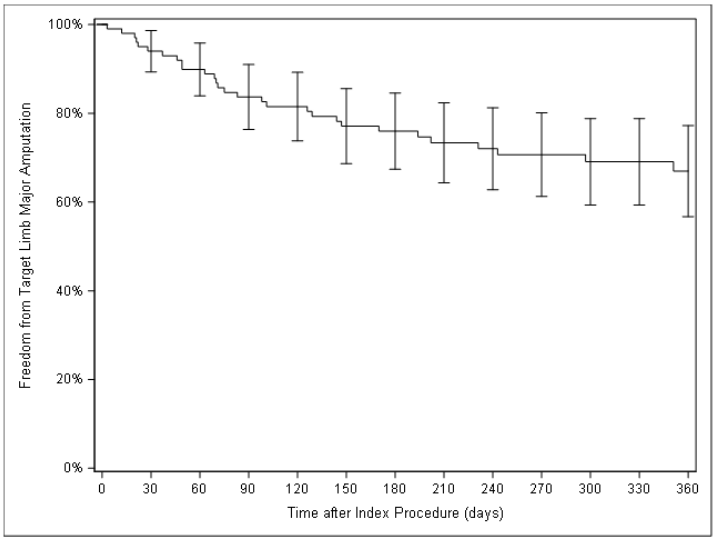

Figure 9: Kaplan Meier Analysis of Limb Salvage

Table 12: Analysis of Limb Salvage over Time

From day X To day Y LimFlow System (N= 105 Subjects)	0 0	1 30	31 60	61 90	91 120	121 150	151 180
# Subjects at Risk	105	105	92	87	78	74	69
# Censored	0	7	1	3	2	1	1
# Events (Major Amputations)	0	6	4	6	2	4	1
Event-free [%]	100.0%	94.0%	89.9%	83.7%	81.5%	77.1%	76.0%
95% Confidence Interval [%]	N/A	87.1% - 97.3%	82.0% - 94.4%	74.7% - 89.7%	72.2% - 87.9%	67.3% - 84.3%	66.0% - 83.3%

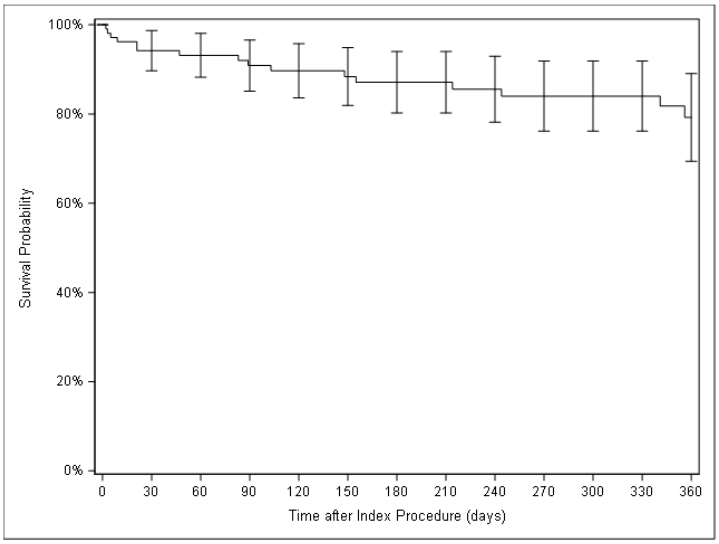

Figure 10: Kaplan Meier Analysis of Survival

Table 13: Analysis of Survival over Time

From day X To day Y LimFlow System (N= 105 Subjects)	0 0	1 30	31 60	61 90	91 120	121 150	151 180
# Subjects at Risk	105	105	92	87	79	75	69
# Censored	0	7	4	6	3	5	1
# Events (Deaths)	0	6	1	2	1	1	1
Event-free [%]	100.0%	94.2%	93.2%	90.9%	89.7%	88.4%	87.1%
95% Confidence Interval [%]	N/A	87.6% - 97.4%	86.2% - 96.7%	83.1% - 95.2%	81.6% - 94.3%	79.9% - 93.4%	78.3% - 92.5%

Bayesian analysis of the Amputation-Free-Survival (AFS) primary endpoint was performed as specified in the study design using the multiple imputation model. The null and alternative hypotheses for the primary endpoint are:

$$H0: \phi \leq 0.54$$
$$HA: \phi > 0.54$$

where ϕ ("phi") is the probability of a subject being alive and free of major amputation at 180 days, and the value 0.54 is a pre-specified performance goal. The performance goal was derived from a literature review conducted by the Yale Cardiovascular Research Group where observed event rates were extracted from each of the relevant studies and combined via a meta-analytic approach to arrive at an estimated historical AFS event rate for patients with no-option CLI. From the posterior mean, the estimated AFS rate at 180 days is 65.8%, with a 95% BCI ranging from 56.5% to 74.5%. The posterior probability that ϕ exceeds the pre-specified performance goal of 0.54 is 0.9931; because this value exceeds the pre-specified threshold of 0.977, the objective is "passed," and the LimFlow System has met its performance goal.

Table 14: Summary of Primary Endpoint Analysis – AFS at 180 days, mITT

Analysis	N	Posterior Mean	95% BCI		Posterior Probability that $\phi > 0.54$
			Lower	Upper	
Primary	105	65.8%	56.5%	74.5%	0.9931
Post-Hoc*	105	65.1%	55.9%	73.9%	0.9903

* An analysis that includes a subject found to have expired after being withdrawn from the study by an investigator 5 days following the study procedure

5. Primary Endpoint Subgroup Analysis

Bayesian subgroup analysis of the primary endpoint was performed as specified in the study design using the multiple imputation model. The primary endpoint was analyzed in these subgroups in the same manner as it was in the full cohort. Numerical summaries of the 180-day AFS for pre-specified subgroups are shown in

Table 15. The AFS rate is consistent across all subgroups, with the exception of subjects on dialysis. There were also small numerical differences based on gender, race, baseline Rutherford category, and presence of diabetes, but the confidence intervals overlap and the sample size is small. These differences are not unexpected in this patient population.

Table 15: Primary Endpoint Analyses by Subgroup

Subgroup	N	AFS[1]	95% BCI	
			Lower	Upper
Age ≤ 70	55	65.7%	52.8%	77.5%
Age > 70	50	65.2%	51.9%	77.5%
Female	33	59.4%	42.8%	75.0%
Male	72	68.4%	57.3%	78.5%
Black or African Descent	16	61.1%	38.3%	81.6%
Caucasian	64	67.6%	55.8%	78.3%
Unknown/Declined	23	59.2%	39.5%	77.4%
Hispanic or Latino	29	62.9%	45.0%	79.0%
Not Hispanic or Latino	76	66.5%	55.7%	76.5%
Diabetes Type I/II	81	61.8%	51.1%	72.0%
Diabetes None	24	76.9%	59.3%	90.6%
Rutherford 5	68	69.2%	57.8%	79.5%
Rutherford 6	37	59.0%	43.4%	73.7%
Dialysis Yes	19	38.1%	19.1%	59.2%
Dialysis No	86	72.2%	62.3%	81.1%

[1]Mean of posterior distribution

F. Secondary Endpoints

Secondary endpoint measures included LimFlow vessel patency, change in Rutherford Class, wound healing, and quality of life.

Vessel patency. Vessel patency status was reviewed via duplex ultrasound at 30 days and 6 months for study subjects. These data, as analyzed by the study imaging core lab, was the foundation of study patency analysis and were combined with CEC-adjudication review of any incidence of occlusion or reintervention without occlusion found outside of protocol-required follow-up visits. The patency endpoint definitions used for the analysis were:

- Primary Patency (P): Defined as absence of occlusion of the endovascular intervention that is maintained without the need for additional or secondary surgical or endovascular procedures, at 30 days and 6 months.

- Primary Assisted Patency (PA): Defined as absence of occlusion of the endovascular intervention that is maintained with the use of additional or secondary surgical or endovascular procedures, as long as occlusion of the primary treated site has not occurred, at 30 days and 6 months.
- Secondary Patency (S): Defined as absence of occlusion of the endovascular intervention that is maintained with the use of additional or secondary surgical or endovascular procedures after occlusion occurs, at 30 days and 6 months.

At 6 months, the percentages of primary patency, primary-assisted patency, and secondary patency were 25.9%, 45.4%, and 64.2%, respectively. Repeat interventions to address native arterial disease and flow optimization within the transcatheter arterialization circuit occurred in 39 patients (37.5%). Additionally, 28 patients lost primary patency due to occlusion without reintervention. Patency was analyzed as a Kaplan Meier analysis as is presented in Figure 11. Rates of event-free survival (subjects remaining patent) are presented in Table 16 below.

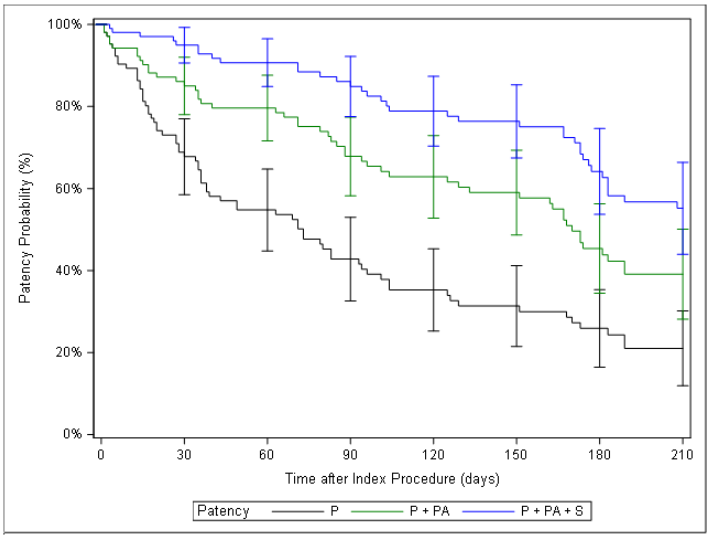

Figure 11: Kaplan Meier Analysis of Patency

Table 16: Analysis of Patency over Time

From day X To day Y LimFlow System (N= 105 Subjects)	0 0	1 30	31 60	61 90	91 120	121 150	151 180
Primary Patency (P)							
# Event Free	105	105	63	48	35	27	23
# Not Evaluable	0	10	3	3	2	1	3
# Loss of Patency	0	32	12	10	6	3	4
Event-free [%]	100.0%	67.7%	54.8%	42.8%	35.2%	31.3%	25.9%
Primary + Primary-Assisted Patency (P+PA)							
# Event free	105	105	79	71	56	49	44
# Not Evaluable	0	11	3	5	3	2	5
# Loss of Patency	0	15	5	10	4	3	10
Event-free [%]	100.0%	85.0%	79.6%	67.8%	62.9%	59.0%	45.4%
Primary + Primary-Assisted + Secondary Patency (P+PA+S)							
# Event free	105	105	89	82	72	64	59
# Not Evaluable	0	11	3	5	3	3	7
# Loss of Patency	0	5	4	5	5	2	9
Event-free [%]	100.0%	94.9%	90.7%	84.9%	78.9%	76.4%	64.2%

Rutherford category. Rutherford category was captured at each timepoint and the change from baseline was evaluated at 30 days, 3 months, and 6 months, as described in Table 17. Table 18 shows the percentage of evaluable subjects with improvement of more than 1 category.

Table 17: Rutherford Category

Rutherford category	Baseline	30 days	3 months	6 months
# subjects evaluated	105	77	74	64
0	0/105 (0.0%)	1/77 (1.3%)	7/74 (9.5%)	9/64 (14.1%)
1	0/105 (0.0%)	0/77 (0.0%)	0/74 (0.0%)	3/64 (4.7%)
2	0/105 (0.0%)	1/77 (1.3%)	1/74 (1.4%)	1/64 (1.6%)
3	0/105 (0.0%)	0/77 (0.0%)	1/74 (1.4%)	0/64 (0.0%)
4	0/105 (0.0%)	3/77 (3.9%)	2/74 (2.7%)	5/64 (7.8%)
5	68/105 (64.8%)	50/77 (64.9%)	48/74 (64.9%)	36/64 (56.3%)
6	37/105 (35.2%)	22/77 (28.6%)	15/74 (20.3%)	10/64 (15.6%)

Table 18: Improvement in Rutherford Category in Evaluable subjects

Characteristic	
30-day improvement in Rutherford $\geq$ 1 class	18.2% (14/77)
3-month improvement in Rutherford $\geq$ 1 class	32.4% (24/74)
6-month improvement in Rutherford $\geq$ 1 class	42.2% (27/64)

Wound healing. Wound healing was analyzed by an independent wound core lab, where wound photos were captured and evaluable. All wound images with sufficient resolution were evaluated. Collection of wound area measurements was challenging due to their susceptibility to lighting, background, plane, distance, angle, circumferential wounds, and the need for the wound to have a healthy tissue border. In addition, wound area data was missing at a high rate for similar reasons and is not included in this summary. The primary wound was determined at baseline, while the qualitative status of healing on all wounds was also analyzed by the core laboratory. During the COVID-19 public health emergency, elective procedures and follow-up were paused or challenging to complete. The protocol was updated to allow images to be taken at home. However, some of these images were not measurable or missing, as detailed in Table 19.

Table 19: Primary Wound Image Status at Each Timepoint

	Baseline	30 days	3 months	6 months
Subjects available for wound follow-up*	105	93	79	68
Evaluable	105	76	72	63
Unevaluable	0	0	0	1
Missing	0	17	7	4

*The number of subjects available for wound follow-up were those that did not fail the primary endpoint (i.e., due to death or major amputation).

Wound healing was determined by an independent wound core lab based on the following criteria:

- Healed: All surfaces of the wound are fully epithelialized; in some cases may have residual scab at the edge of epithelialization: this is distinct from a wound eschar but there is no exposed surface of unepithelialized tissue. Wound size is 0.
- Healing: Evidence of granulation tissue formation; epithelialization of wound edges is apparent; contraction of wound edges may be evident; in early stages of healing the granulation tissue may be less apparent or less robust (pink as compared to red) but the wound base is generally clean with no exudate or evidence of purulence; this term was also used for minor amputation sites that have characteristics of healthy wound tissue. Wound area is decreased in size or stable.
- Stable: No evidence of increasing granulation tissue formation, wound contraction, or increased epithelialization, but also with no evidence of worsening necrosis, exudate, or purulence/infection. Wound area not appreciably changed in size.
- Worsening: Increasing evidence of necrosis, exudate, or purulence; evidence of eschar development or increasing ischemic changes of surrounding skin and soft tissues; this term was used for minor amputations with non-healing wound bases. Wound area is unchanged or increased in size.

The results for wound healing for the primary wound in evaluable subjects are provided in Table 20. In subjects with evaluable wounds, over half were worsening at 30 days. At 6 months, 25% of evaluable wounds were healed.

Table 20: Primary Wound Healing in Evaluable Subjects

Status	30 days	3 months	6 months
# Evaluable	76	72	63
Healed	3	6	16
Healing	9	28	32
Stable	24	16	7
Worsening	40	22	7

G. Quality of Life Pain Results

Study subjects reported pain at each follow-up visit on a scale of 1-10. At baseline, 57/92 subjects had a pain score of 5 or greater, while at 6-months, the majority of subjects (45/65, 69.0%) had a pain score 4 or less.

H. Device Malfunctions

The definition of device malfunction in the PROMISE II study is any occurrence of equipment not functioning or operating as intended. There were 14 cases of device malfunction reported in the study with the LimFlow stent, none of which resulted in an adverse event.

SUPPLEMENTARY DATA – PROMISE I TRIAL

The PROMISE I trial (NCT03124875) was the early feasibility study performed on the first generation of the LimFlow System which comprised of arterial and venous crossing catheters, an ultrasound system utilized in the establishment of the arteriovenous crossing, valvulotome, and the first and second generation of the LimFlow self-expanding conical and cylindrical stent grafts. The PROMISE I Study was a prospective, single-arm, multi-center feasibility study of the LimFlow System that enrolled 32 subjects in the United States under IDE# G160156. The objective of the PROMISE I trial was to evaluate the feasibility, safety, and effectiveness of the LimFlow System in creating a below-the-knee arteriovenous fistula for venous arterialization in subjects with chronic limb-threatening ischemia.

The study primary endpoint was amputation-free survival (AFS) at 30 days, defined as the percentage of subjects who survived with limb salvage. Limb Salvage was defined as freedom from above-ankle amputation of the index limb, and survival was defined as freedom from all-cause mortality. Descriptive statistics are provided as no hypothesis testing was performed due to the small sample size.

The study's secondary safety endpoint was Amputation-Free Survival at 6-months with the same definitions for AFS and Limb Salvage as the primary safety endpoint.

There were multiple secondary effectiveness endpoints that were evaluated in the study INCLUDING Primary Patency at 30 days, Primary Patency at 6 months, Secondary Patency at 6 months, Deterioration in Renal Function at 6 months, Limb Salvage, Technical Success, Procedural Success, and Wound Healing.

The study was successful in demonstrating feasibility with positive outcomes on all endpoints. A brief overview of the PROMISE I results are provided below in Table 21.

Table 21: PROMISE I Results

KEY PERFORMANCE DATA	Kaplan Meier Estimates	Rate n/N (%)
Technical Success[1]	--	31/32 (96.9%)
Procedural Success[2]	--	24/31 (77.4%)
PRIMARY & SECONDARY SAFETY ENDPOINTS		
30-day Amputation-Free Survival (AFS) [95% CI]	90.6% [73.7% - 96.9%]	28/31 (90.3%)
30-day Survival	100.0%	28/28 (100.0%)
30-day Limb Salvage	90.6%	28/31 (90.3%)
6-month Amputation-Free Survival (AFS) [95% CI]	73.8% [54.4% - 86.0%]	22/30 (73.3%)
6-month Survival	96.3%	22/23 (95.7%)
6-month Limb Salvage	76.7%	22/29 (75.9%)
SECONDARY ENDPOINTS (SAFETY)		
12-month AFS	69.5%	20/29 (69.0%)
12-month Survival	91.6%	20/22 (90.9%)
12-month Limb Salvage	75.9%	22/27 (75.9%)
24-month AFS	58.7%	16/28 (57.1%)
24-month Survival	77.3%	16/21 (76.2%)
6-month Renal Deterioration due to Contrast-Induced Nephropathy	--	3/32 (9.4%)
SECONDARY ENDPOINTS (PERFORMANCE)		
30-day Primary Patency	73.2%	22/30 (73.3%)
6-month Complete Wound Healing	19.0%	5/20 (25%)
12-month Complete Wound Healing	58.7%	9/16 (56%)

[1]Technical Success was defined as: percentage of subjects with completion of the endovascular procedure and immediate morphological success with successful placement of the arterial and venous catheters in the desired location in the limb, and ability to place the stent graft.

[2]Procedural Success was defined as: percentage of subjects with combination of technical success, and absence of all-cause death, above-ankle amputation or clinically driven major re-intervention of the stent graft at 30 days.

Technical success was achieved in 31 cases resulting in a 96.9% technical success rate. There was one case of technical failure in 32 treated subjects. Arterial and venous catheters were successfully placed and initial arterio-venous crossing and wire placement were successful. Work in tortuous venous anatomy led to crossing wire being removed completely from the circuit and attempts to regain arterio-venous crossing were unsuccessful. The remaining LimFlow procedure was aborted prior to the use of valvulotomy and placement of stents.

Procedural success was achieved in 24 subjects (77.4%), out of 31 subjects available for follow-up or who failed the procedural success endpoint prior to 30 days.

The study primary endpoint of amputation-free-survival (AFS) at 30 days was 90.6%, and secondary endpoint of AFS at 6-months was 73.8%. This was well-maintained over the longer-duration with AFS at 12 and 24-months 69.5% and 58.7%, respectively. Limb salvage was 90.6% and 76.7% at 30 days and 3-months, respectively, with no incidents of above-ankle amputation throughout the rest of the 24 months of follow-up. All AFS events after 3-months were exclusively deaths mostly due to pre-existing medical conditions unrelated to CLTI.

An independent wound core lab reviewed wound images from baseline and all follow-up time-points, as available, to determine the healing status. Complete wound healing was 58.7% at 12-months.

The PROMISE I trial was successful in its objective to establish feasibility and demonstrate initial safety and effectiveness of the LimFlow System in creating a below-the-knee arteriovenous fistula for venous arterialization in subjects with chronic limb-threatening ischemia.

CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The nonclinical and preclinical testing conducted on the stent grafts, delivery system, and accessories demonstrated that the performance characteristics of the device met the product specifications and are acceptable for clinical use.

The prospective single-arm, multi-center study (PROMISE II) was designed to evaluate the transcatheter arterialization of the deep veins (TADV) via the LimFlow System in subjects with no-option CLTI. No-option CLTI was defined as either a) absence of a usable pedal artery target (endovascular or surgical approach), or b) the presence of a pedal artery target with absence of a viable single-segment vein in either lower extremity or either arm that could be used for autogenous vein conduit. The study demonstrated technical success in 104/105 (99.0%) subjects. The primary safety and effectiveness endpoint was amputation-free survival at 6 months. At 6 months, 67 subjects remaining in the study were event free. The 6-month amputation-free survival rate estimated by the mean of the posterior distribution is 65.8%, with 95% Bayesian credible interval (BCI) of (0.565-0.745). The posterior probability that this rate exceeds the performance goal of 0.54 is 0.993, exceeding the study's pre-defined success criterion of 0.977. As estimated by Kaplan-Meier method, 6-month amputation-free survival is 66.1%. For minor amputations, 29.5% had toe amputations and 40% had amputations above the toe and below the ankle. Primary patency was 25.9% at 6 months, and secondary patency was 64.2%. Patients generally experienced improvements in Rutherford category, wound improvement, and reduced pain as compared to typical expectations for no-option CLTI patients.

The PROMISE II trial enrolled subjects that were representative of real-world patients, including those with dialysis-dependence and Rutherford class 5 or 6 wounds, who are routinely excluded from vascular device studies. Beyond routine co-morbidities including diabetes, 74.3% of the subjects had a history of prior unsuccessful revascularization of the index limb, indicating a complex cohort of patients at risk of major amputation.

B. Safety Conclusions

Adverse event rates were consistent with expectations for this high-risk population, which has many comorbidities, and events align with the underlying baseline risk factors and medical history for this population. Freedom from contrast-induced nephropathy was reported in 98.1% of subjects and 6-month limb-salvage was 76.0%. Overall, the clinical study results are adequate to provide a reasonable assurance of the safety of the LimFlow System in treating no-option CLTI by creating an arteriovenous connection in the below-the-knee vasculature.

PATENT INFORMATION

Please see www.LimFlow.com/patents

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Symbols Used on Labeling

	Manufacturer		Caution when operating the device
	Keep Dry		Sterilized using ethylene oxide
	Keep away from sunlight		Consult electronic instructions for use
	Do not use if package is damaged		No latex
	Do not re-use		MR Conditional
	Do not resterilize		Catalog Number
	Prescription only		Batch Code
	Non-pyrogenic		Use-by Date
	Single Sterile Barrier System		Unique device identifier