Esprit™ BTK
Everolimus Eluting Resorbable Scaffold System

℞ ONLY

INSTRUCTIONS FOR USE

Table of Contents

This Instructions for Use (IFU) is provided for general information regarding the Esprit™ BTK Everolimus Eluting Resorbable Scaffold System.

1.0 DEVICE DESCRIPTION

The Esprit™ BTK Everolimus Eluting Resorbable Scaffold System (Esprit™ BTK System) is composed of a balloon expandable scaffold and a delivery system. The Esprit™ BTK Scaffold is a resorbable polymeric scaffold with a drug and resorbable polymeric coating. The Esprit BTK Scaffold is temporary and will resorb over time.

1.1 Device Component Description

The characteristics of the Esprit BTK System are summarized in *Table 1.1-1*.

Table 1.1-1: Product Description

Product Name	**Esprit BTK System**
Scaffold Lengths (mm)	9, 12, 15, 18, 23, 28, 33, 38
Scaffold Diameters (mm)	2.50, 2.75, 3.00, 3.50, 3.75
Scaffold Backbone Material	poly(L-lactide) (PLLA)
Drug Component	A blend of the antiproliferative drug everolimus and polymer poly(D, L-lactide) (PDLLA) in a 1:1 ratio with 100 µg/cm^2 of everolimus.
Delivery System Working Length	145 cm
Delivery System Design	Rapid exchange (RX): Single access port to inflation lumen. A shaft material change from gray stainless steel material to orange polymer material denotes the guide wire exit notch on the delivery system. Two proximal delivery system shaft markers are located at 95 cm and 105 cm proximal to the distal tip.
Delivery System Balloon Markers	Two radiopaque markers, located underneath the balloon, fluoroscopically mark the working length of the balloon and the location of the undeployed scaffold on the scaffold delivery system.
Balloon Inflation Pressure	***In vitro* Nominal Pressure: 9 atm (912 kPa) Rated Burst Pressure (RBP): 16 atm (1621 kPa)
*Minimum Introducer Sheath Capability Inner Diameter (ID) (F/inches/mm)	5F / 0.070” / 1.8 mm
Guide Wire	Maximum Diameter: 0.014" (0.36 mm) Minimum Length: 175 cm

* See individual manufacturer specifications for (F) equivalent.

** Ensure full deployment of the scaffold (see *Section 12.6 Deployment Procedure*).

Note: Deployment pressures should be based on lesion characteristics.

1.1.1 Scaffold Backbone

The Esprit BTK Scaffold backbone is fabricated from poly(L-lactide) (PLLA). PLLA is a fully resorbable semicrystalline polymer which is synthesized from the cyclic L-lactide dimer composed of two L-lactic acid units.

1.1.2 Scaffold Radiopaque Markers

The scaffold contains four radiopaque platinum markers, two located at each end ring. These radiopaque markers mark the scaffold length prior to deployment and after expansion in the artery. The Esprit BTK Scaffold itself is not visible under fluoroscopy.

1.1.3 Drug Component Description

The Esprit BTK Scaffold is coated with everolimus (active pharmaceutical ingredient) and a resorbable polymer – poly(D, L-lactide) (PDLLA) (inactive ingredient).

1.1.3.1 Everolimus

Everolimus is the active pharmaceutical ingredient (API) in the Esprit BTK Scaffold. It is a semi-synthetic macrolide immunosuppressant, synthesized by chemical modification of rapamycin (sirolimus). The everolimus chemical name is 40-O-(2-hydroxyethyl)-rapamycin and the chemical structure is shown in *Figure 1.1.3.1-1* below.

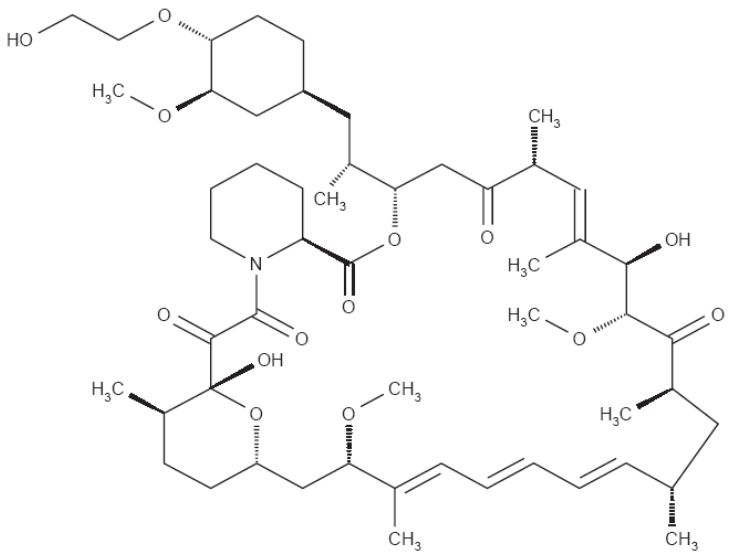


Figure 1.1.3.1-1: Everolimus Chemical Structure

1.1.3.2 Inactive Ingredients – Resorbable Polymer – poly(D, L-lactide) (PDLLA)

The Esprit BTK Scaffold coating contains the inactive ingredient, poly(D, L-lactide) (PDLLA), a polymer that adheres to the scaffold to provide controlled delivery of the antiproliferative drug everolimus. The PDLLA is mixed with everolimus (1:1 w/w) and applied to the entire scaffold surface.

1.1.3.3 Product Matrix and Everolimus Content

The scaffold sizes and nominal everolimus content on the scaffold based on the established dose density of 100 µg/cm^2 are shown in *Table 1.1.3.3-1*.

Table 1.1.3.3-1: Drug Content in Esprit BTK Scaffold

Scaffold Diameter (mm)	Scaffold Length (mm)	Nominal Everolimus Content (µg)
2.50, 2.75	9	69
2.50, 2.75	12	93
2.50, 2.75	15	116
2.50, 2.75	18	139
2.50, 2.75	23	178
2.50, 2.75	28	217
2.50, 2.75	33	256
2.50, 2.75	38	295
3.00	9	75
3.00	12	98
3.00	15	121
3.00	18	144
3.00	23	189
3.00	28	227
3.00	33	273
3.00	38	311
3.50	9	94
3.50	12	119
3.50	15	153
3.50	18	188
3.50	23	239
3.50	28	290
3.50	33	341
3.50	38	391
3.75	9	89
3.75	12	125
3.75	15	161
3.75	18	188
3.75	23	242
3.75	28	296
3.75	33	350
3.75	38	404

2.0 HOW SUPPLIED

Sterile – This device is sterilized with electron beam radiation. Non-pyrogenic. Do not use if the package is open or damaged.

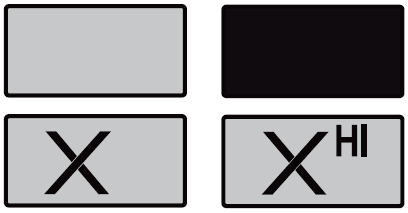
This single-use device cannot be reused on another patient, as it is not designed to perform as intended after the first usage. Changes in mechanical, physical, and / or chemical characteristics introduced under conditions of repeated use, cleaning, and / or re-sterilization may compromise the integrity of the design and / or materials, leading to contamination due to narrow gaps and / or spaces and diminished safety and / or performance of the device. Absence of original labeling may lead to misuse and eliminate traceability. Absence of original packaging may lead to device damage, loss of sterility, and risk of injury to the patient and / or user.

Contents – One (1) Esprit™ BTK Everolimus Eluting Resorbable Scaffold System; one (1) temperature monitor.

Storage – Keep dry. Keep away from sunlight. Do not separate the product from temperature monitor until ready for use. Store at or below 25°C (77°F); excursions permitted to 30°C (86°F).

Temperature monitor – A non-sterile temperature monitor included in the package is for the shipping and storage of the Esprit™ BTK System. Before use of the Esprit BTK System, check the temperature monitor located through window in the back of the product box. The indicator should only show a check mark as indicated in the digital display (*Table 2.0-1 A*). If any other screen is present (*Table 2.0-1 B*), do not use the product.

Table 2.0-1: Temperature Monitor Window Indicator Options, Instructions for Use and Disposal Instructions

	Window Indicator	Instructions for Use	Disposal Instructions
A		Use	 The temperature monitor is a battery-powered device. Remove temperature monitor from carton and dispose in accordance with local regulations.
B		Do not use	

3.0 INDICATIONS

The Esprit™ BTK Everolimus Eluting Resorbable Scaffold System is indicated for improving luminal diameter in infrapopliteal lesions in patients with chronic limb-threatening ischemia (CLTI) and total scaffolding length up to 170 mm with a reference vessel diameter of ≥ 2.5 mm and ≤ 4.00 mm.

4.0 CONTRAINDICATIONS

The Esprit™ BTK Everolimus Eluting Resorbable Scaffold System is contraindicated for use in:

- Patients who cannot tolerate, including allergy or hypersensitivity to, procedural anticoagulation or the post-procedural antiplatelet regimen.

- Patients with hypersensitivity or contraindication to everolimus or structurally related compounds or known hypersensitivity to scaffold components poly(L-lactide), poly(D, L-lactide), and platinum.

5.0 WARNINGS

- **This device is intended for single use only.** Do not reuse, reprocess, or re-sterilize. Note the product "Use-by" date on the package. Reuse, reprocessing, or re-sterilization may compromise the structural integrity of the device and / or delivery system and / or lead to device failure, which may result in patient injury, illness, or death. Reuse, reprocessing, or re-sterilization may also create a risk of contamination of the device and / or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s) from one patient to another. Contamination of the device and / or delivery system may lead to injury, illness, or death of the patient.

- The Esprit™ BTK System is intended to perform as a system. The scaffold should not be removed for use with other dilatation catheters.

- The Esprit BTK System should not be used in conjunction with other non-everolimus drug-eluting devices in the same vessel as the Esprit™ BTK Scaffold.

- It is not recommended to use this scaffold to treat lesions located at any joint or other hinge points, such as the knee or ankle. The recommended region for below-the-knee (BTK) treatment with the Esprit BTK Scaffold is the infrapopliteal arteries at a location ≥ 10 cm above the proximal margin of the ankle mortise. The Esprit BTK Scaffold has not been tested for use outside the recommended implant locations.

- This product should not be used in patients with aneurysms immediately adjacent to the scaffold implantation site.

- Insertion of the Esprit BTK System and implantation of the scaffold should be performed only under fluoroscopic observation with radiographic equipment providing high resolution images.

- **Quantitative imaging is strongly recommended to accurately measure and confirm appropriate vessel sizing (reference vessel diameter ≥ 2.5 mm).** If quantitative imaging determines a vessel size < 2.5 mm, do not implant the Esprit BTK Scaffold.

- Adequate lesion preparation prior to scaffold implantation is required to ensure safe delivery of the scaffold across the target lesion. It is not recommended to treat patients having a lesion that prevents complete inflation of an angioplasty balloon.

- **Successful pre-dilatation with residual diameter stenosis of < 30% by visual estimation is required for treatment of the target lesion; < 20% by visual estimation is preferred.**

- Ensure the scaffold is not post-dilated beyond the allowable expansion limits (see *Section 12.7 Further Expansion of the Deployed Scaffold*).

- Use of appropriate anticoagulant and / or antiplatelet therapy per standard of care is recommended for use of this scaffold system.

- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy.

- Judicious selection of patients is necessary, since the use of this device carries the associated risk of scaffold thrombosis, vascular complications, and / or bleeding events.

- Once fully deployed, the scaffold cannot be repositioned.

- The Esprit BTK Scaffold is coated with an everolimus and polymer coating for the full implant scaffold length. The distal and intermediate portions of the delivery system, the tip, and tapers of the balloon are coated with HYDROCOAT™ Hydrophilic Coating. See *Section 12.0 Clinician Use Information* for further information on how to prepare and use this device to ensure it performs as intended. Failure to abide by the warnings in this labeling might result in damage to the device coating, which may necessitate intervention or result in serious adverse events.

6.0 PRECAUTIONS

6.1 General

- Scaffold placement should not be performed in patients with known allergies to contrast agent that cannot be medically managed.

- It is not recommended to treat patients having a lesion with excessive tortuosity proximal to or within the lesion.

- When multiple scaffolds are required, only combinations of Esprit™ BTK Scaffolds must be used. Any potential interaction with other drug-eluting or coated devices has not been evaluated.

- The delivery system is intended for deployment of the scaffold only and should not be used to dilate other locations.

- Estimated vessel reference size should not be less than 2.5 mm in diameter or greater than 4.0 mm in diameter.

6.2 Delivery System Handling

- Do not remove the scaffold from its delivery system, as removal may damage the scaffold and / or lead to scaffold embolization. The Esprit™ BTK System is intended to perform as a system.

- Carefully inspect the Esprit BTK System prior to use to verify that the scaffold has not been damaged in shipment and that the device dimensions are suitable for the specific procedure. Take care to avoid unnecessary handling.

- Do not “roll” the mounted scaffold with your fingers, as this action may loosen the scaffold from the delivery balloon.

- Do not use if the scaffold is partially deployed upon removal from the package or before starting the deployment procedure.

- Do not dilate the scaffold beyond the dilatation limit indicated in *Table 12.7-1*.

- Never advance the Esprit™ BTK Scaffold delivery system without the guide wire extending from the tip.

- Refer to the instructions for use supplied with any interventional devices to be used in conjunction with Esprit BTK System for their intended uses, contraindications, and potential complications.

6.3 Scaffold Handling

- Implantation of the scaffold should be performed **only** by physicians who have received appropriate training.

- As with all catheter-based procedures, scaffold placement should be performed at facilities where patient can be prepared for necessary intervention and / or surgical removal of the device and vessel repair as per facility protocol.

- To confirm sterility has been maintained, ensure that the package sterile barrier has not been opened or damaged prior to use.

- Careful assessment of the target lesion reference vessel diameter and selection of the appropriate scaffold diameter relative to the target lesion reference vessel diameter are required to minimize potential damage to the scaffold during post-dilatation and to ensure adequate scaffold apposition and an appropriate post-implantation minimum lumen diameter.

- Use introducer sheaths which have lumen sizes that are suitable to accommodate the scaffold system.

- Care should be taken to control the introducer sheath tip during scaffold delivery, deployment, and balloon withdrawal. Before withdrawing the scaffold delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid introducer sheath movement into the vessel and subsequent arterial damage.

- Special care must be taken not to handle or in any way disrupt the scaffold from the balloon. This is most important during catheter removal from packaging, placement over the guide wire, and advancement through the introducer sheath and hemostatic valve.

- **Do not manipulate, touch, or handle the scaffold**, as this may cause coating damage, contamination, or dislodgement of the scaffold from the delivery balloon.

- Avoid wiping the device with dry gauze or excessive wiping of the device as this may damage the device coating.

- Avoid using alcohol, antiseptic solutions, or other solvents to pre-treat the device because this may cause unpredictable changes in the coating which could affect the device safety and performance.

- Avoid soaking the Esprit BTK Scaffold. See instructions in *Section 12.4.3 Guide Wire Lumen Flush*.

- Use only the appropriate balloon inflation media. Do not use air or any gaseous medium to inflate the balloon, as this may cause uneven expansion and difficulty in deployment of the scaffold. If gaseous medium is used and balloon rupture occurs, there is the potential of causing air embolism and / or vessel injury.

6.4 Scaffold Placement

- Always use an appropriately sized introducer sheath. Inappropriately sized introducer sheath usage may cause device damage.

- **Do not prepare or pre-inflate the delivery system prior to scaffold deployment, other than as directed**. Use the technique described in *Section 12.4.4 Delivery System Preparation*.

- Pre-dilatation should be performed with an angioplasty balloon. Cutting or scoring balloons can be used per physician discretion, if the lesion appears to be mildly calcified.

- Failure to pre-dilate the vessel may impair nominal / optimal scaffold delivery.

- When pre-dilatation is performed, an appropriate balloon size should be used based on patient and lesion characteristics. Failure to do so may increase the difficulty of scaffold placement and cause procedural complications.

- When introducing the delivery system into the vessel, do not induce negative pressure on the delivery system. This may cause dislodgement of the scaffold from the balloon.

- Do not torque the delivery system catheter more than one (1) full turn.

- Use caution when advancing the Esprit BTK Scaffold across the lesion. Multiple attempts to cross a lesion may lead to scaffold damage or dislodgement.

- Implanting a scaffold may lead to dissection of the vessel distal and / or proximal to the scaffold, requiring additional intervention.

  Note: In cases of bailouts, bailout treatment of the target lesion can be done using the

Esprit BTK Scaffold of the appropriate length. If an appropriate length Esprit BTK Scaffold is not available, physicians should use standard of care.

- In the event of abrupt vessel closure / total occlusion of the scaffold, a bailout implant may be inserted and deployed within the scaffold such that the Esprit BTK Scaffold is completely covered by the bailout implant.

  Note: It is recommended that bailouts for abrupt closure / total occlusion of the scaffold be done with a metallic everolimus-eluting stent of appropriate size.

- An unexpanded scaffold may be retracted into the introducer sheath **one time only**. An unexpanded scaffold should not be reintroduced into the artery once it has been pulled back into the introducer sheath. Subsequent movement in and out through the distal end of the introducer sheath should not be performed, as the scaffold may be damaged or dislodged during retraction back into the introducer sheath.

- Should **resistance** be felt **at any time** during removal of the undeployed Esprit BTK System, refer to the steps provided in *Section 6.6 Scaffold / System Removal*.

- Do not expand the scaffold if it is not properly positioned in the vessel (see *Section 6.6 Scaffold / System Removal*)

- Scaffolding across a major bifurcation may hinder or prevent future diagnostic or therapeutic procedures.

- The inflated balloon diameter of the system used to deploy the scaffold should approximate the diameter of the vessel. To ensure full expansion of the scaffold, the balloon should be inflated to a minimum of nominal pressure.

- **Do not exceed the rated burst pressure (RBP) as indicated on the product label.** Monitor balloon pressures during inflation. Use of pressures higher than RBP specified on the product label may result in a ruptured balloon, with possible intimal damage and dissection.

- Although the scaffold delivery system balloon is strong enough to expand the scaffold without rupture, a circumferential balloon tear distal to the scaffold and prior to complete scaffold expansion could cause the balloon to become tethered to the scaffold, requiring surgical removal. In case of balloon rupture, it should be withdrawn and, if necessary, a new dilatation catheter should be exchanged over the guide wire to complete the expansion of the scaffold.

- Post-dilatation is strongly recommended for optimal scaffold apposition. When performed, post-dilatation should be performed at high pressure (> 16 atm) with a non-compliant balloon up to 0.5 mm larger than the nominal scaffold diameter.

- Under-expansion of the scaffold may result in scaffold movement. Care must be taken to properly size the scaffold to ensure that the scaffold is in full contact with the arterial wall upon deflation of the balloon. All efforts should be made to ensure that the scaffold is not under-dilated. See *Section 12.7 Further Expansion of the Deployed Scaffold*.

- Balloon dilatation of a deployed Esprit BTK Scaffold cell may cause scaffold damage.

- Scaffold retrieval methods (use of additional wires, snares, and / or forceps) may result in additional trauma to the peripheral vasculature and / or the vascular access site. Complications may include bleeding, hematoma, or pseudoaneurysm.

- Use an appropriately sized non-drug coated balloon to pre-dilate the lesion. When treating a long lesion, scaffold the distal portion of the lesion prior to scaffolding the proximal portion of the lesion. Scaffolding in this order obviates the need to cross the proximal scaffold during placement of the distal scaffold, and reduces the chance of damaging or dislodging the proximal scaffold.

- Ensure that the scaffolded area covers the entire lesion / dissection site and that no gaps exist between scaffolds.

- The extent of the patient's exposure to drug and polymer is directly related to the number of scaffolds implanted. The safety of everolimus, polymer, and polymer breakdown products was evaluated in pre-clinical studies and the biocompatibility assessment of the Esprit BTK Scaffold.

- No safety or toxicity concerns were related to everolimus, polymer or polymer degradants, or any chemicals generated through the life-cycle of the Esprit BTK Scaffold through dosing up to 170 mm scaffolding length which is equivalent to 1790 µg drug dose.

- The safety and effectiveness of the Esprit BTK Scaffold in patients with prior brachytherapy of the target lesion or the use of brachytherapy for treated-site restenosis in the Esprit BTK Scaffold have not been established. Both vascular brachytherapy and the Esprit BTK Scaffold alter arterial modeling. The potential combined effect on arterial remodeling by these two treatments is not known.

6.5 Use in Conjunction with Other Procedures

- The safety and effectiveness of the Esprit BTK System have not been established in clinical trials with the use of either mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser atherectomy catheters.

6.6 Scaffold / System Removal

- Scaffold system removal prior to scaffold deployment:

  If removal of a scaffold system is required prior to deployment, ensure that the introducer sheath is coaxially positioned relative to the scaffold system and cautiously withdraw the scaffold system into the introducer sheath. Should **unusual resistance** be felt **at any time** when withdrawing the scaffold into the introducer sheath, the scaffold system, and the introducer sheath should be **removed as a single unit**. This should be done under direct visualization with fluoroscopy. The scaffold cannot be reinserted.

- Withdrawal of the scaffold delivery system / post-dilatation balloon from the deployed scaffold:

  1. Deflate the balloon by pulling negative on the inflation device. Larger and longer balloons will take more time (up to 30 seconds) to deflate than smaller and shorter balloons. Confirm balloon deflation under fluoroscopy and wait 10 – 15 seconds longer.

2. Position the inflation device to “negative” or “neutral” pressure.
3. Open the rotating hemostatic valve (if used).
4. Stabilize introducer sheath position and anchor in place. Maintain guide wire placement across scaffold segment.
5. Gently remove the scaffold delivery system / post-dilatation balloon with slow and steady pressure.
6. Tighten the rotating hemostatic valve (if used).

Notes:

1. **If during withdrawal of the catheter from the deployed scaffold, resistance is encountered, use the following steps to improve balloon rewrap:**
    - Re-inflate the balloon up to nominal pressure, deflate and change pressure to neutral.
    - Repeat steps 1 through 4 above.
2. After successful withdrawal of the balloon from the deployed scaffold, should **any resistance** be felt **at any time** when withdrawing the scaffold delivery system or post-dilatation balloon into the introducer sheath, **remove the entire system as a single unit**.

- Failure to follow the steps and / or applying excessive force to the delivery system can potentially result in loss of or damage to the scaffold and / or delivery system components.
- If it is necessary to retain guide wire position for subsequent artery / lesion access, leave the guide wire in place and remove all other system components.

6.7 Post-Implantation

- **If necessary to cross a newly deployed scaffold** with a guide wire, balloon, delivery system, or imaging catheters, exercise care to avoid disrupting the scaffold geometry.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the scaffold. The long-term outcome following repeat dilatation of scaffolds is unknown at present.
- If the patient requires imaging, see *Section 6.8 Magnetic Resonance Imaging (MRI) Safety Information*.

CAUTION: Information must be supplied to the patient with an implanted device by way of an implant card.

6.8 Magnetic Resonance Imaging (MRI) Safety Information

MR Conditional

MRI Safety Information

Non-clinical testing has demonstrated the Esprit BTK Scaffold is MR Conditional. A person with the Esprit BTK Scaffold may be safely scanned under the following conditions. Failure to follow these conditions may result in injury.

Device Name	Esprit BTK Scaffold
Static Magnetic Field Strength (B_0)	7 Tesla or less

The Esprit BTK Scaffold should not migrate in this MRI environment. MRI at 7 Tesla or less may be performed immediately following the implantation of the Esprit BTK Scaffold.

6.9 Use in Special Populations

6.9.1 Pregnancy

The safety and effectiveness of the Esprit BTK Scaffold in pregnant patients have not been established.

Pregnancy Category C: *See also Section 6.12.4 Pregnancy*.
This Esprit™ BTK Everolimus Eluting Resorbable Scaffold System and everolimus have not been tested in pregnant or nursing women or in men intending to father children. Effects on the developing fetus have not been studied[1]. While there is no contraindication, the risks and reproductive effects are unknown at this time.

6.9.2 Lactation

The safety and effectiveness of the Esprit BTK Scaffold in lactating mothers have not been established.

See also *Section 6.12.5 Lactation*. It is unknown whether everolimus is distributed in human milk. A decision should be made whether or not to discontinue nursing prior to scaffold implantation, considering the importance of the scaffold to the mother.

[1] Certican‡ UK SmPC, Afinitor‡ UK SmPC, Votubia‡ UK SmPC, Afinitor‡ US label, and Zortress‡ US label. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SmPC / labels.

6.9.3 Gender

The assessment of gender effect in the LIFE-BTK Randomized Controlled Trial (RCT) for the primary effectiveness endpoint of limb salvage and primary patency at 1 year showed no significant treatment interaction by gender (interaction p-value = 0.7546). Within each gender subgroup, the observed 1-year primary effectiveness endpoint still demonstrated statistically significant superiority compared to the percutaneous transluminal angioplasty (PTA) arm. Also, the observed rate for the primary safety endpoint at 6 months within the subgroup was comparable between the two treatment arms with no statistically significant difference.

6.9.4 Ethnicity and Race

The assessment of race (White vs. Black or African American vs. other race) effect for the primary effectiveness endpoint in the LIFE-BTK RCT showed no significant treatment interaction by race (interaction p-value = 0.2041). Within each race subgroup, the observed 1-year primary effectiveness endpoint still demonstrated statistically significant superiority compared to the PTA arm. In addition, the observed rate for the primary safety endpoint at 6 months within the subgroup was comparable between the two treatment arms with no statistically significant difference.

The assessment of ethnicity (Hispanic or Latino vs. non-Hispanic or non-Latino) effect in the LIFE-BTK RCT was not a pre-specified analysis. A post-hoc analysis was conducted and showed that event rates for the primary safety and primary effectiveness endpoints in the Hispanic or Latino population were consistent with event rates observed in the overall LIFE-BTK RCT population. In the Hispanic or Latino population, primary safety endpoint rates were 89.3% and 100.0%, and primary effectiveness endpoint rates were 74.1% and 40.0% in the Esprit BTK and PTA arms, respectively.

6.9.5 Pediatric Use

The safety and effectiveness of Esprit BTK Scaffold in pediatric patients have not been established.

6.9.6 Geriatric Use

The LIFE-BTK RCT had a median subject age of 73 years. There was no upper age limit for trial eligibility. Within the ≥ 65 years subgroup, the observed rate for the primary effectiveness endpoint of limb salvage and primary patency at 1 year was numerically higher in Esprit BTK arm compared to the PTA arm (73.5% vs 40.4%), whereas the observed rate for the primary safety endpoint at 6 months was comparable between the two treatment arms with no statistically significant difference (97.6% for Esprit BTK arm vs 100.0% for PTA arm).

6.10 Lesion / Vessel Characteristics

The safety and effectiveness of Esprit BTK Scaffold have not been established for patient populations with the following characteristics:

- BTK artery with reference vessel diameters < 2.5 mm or > 4.0 mm
- Lesions that would require a total of > 170 mm of scaffolds for treatment
- Previously stented lesions
- Lesions with severe calcification
- Bifurcation lesions that required scaffold placement in both branches

6.11 Off-Label Use

Compared to use within the specified indications for use, the use of the Esprit BTK System in patients and lesions outside of the labeled indication, may have an increased risk of adverse events, including scaffold thrombosis, or scaffold embolization.

6.12 Drug Interactions

6.12.1 Interactions with Drug or Other Substances

Everolimus is extensively metabolized by the cytochrome P450 3A4 (CYP3A4) in the liver and to some extent in the intestinal wall and is a substrate for the counter transporter P-glycoprotein (PgP). Therefore, absorption and subsequent elimination of everolimus may be influenced by drugs that also affect CYP3A4 and PgP pathways. Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Formal drug interaction studies have not been performed with the Esprit BTK Scaffold because of limited exposure to everolimus eluted from the scaffold (see *Section 7.2 Pharmacokinetics*). Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place the Esprit BTK Scaffold in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received an Esprit BTK Scaffold.

Everolimus, when prescribed as an oral medication, may interact with the following drugs or foods including but not limited to:

- CYP3A4 / PgP isozyme inhibitors
    - Antifungal agents (e.g., fluconazole, ketoconazole, itraconazole, posaconazole, voriconazole)
    - Macrolide antibiotics (e.g., erythromycin, clarithromycin, telithromycin)
    - Calcium channel blockers (e.g., verapamil, nicardipine, diltiazem)
    - Cannabidiol
    - Protease inhibitors (e.g., ritonavir, atazanavir, saquinavir, darunavir, indinavir, nelfinavir, amprenavir, fosamprenavir)
    - Other (e.g., cyclosporine, nefazodone, cisapride, metoclopramide, bromocriptine, cimetidine, danazol, sildenafil, terfenadine, astemizole, grapefruit / grapefruit juice, digoxin)

- CYP3A4 / PgP isozyme inducers
    - Antibiotics (e.g., rifampin, rifabutin, ciprofloxacin, ofloxacin)
    - Anticonvulsants (e.g., carbamazepine, phenobarbital, phenytoin)
    - Non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz, nevirapine)
    - Glucocorticoids (e.g., dexamethasone, prednisone, prednisolone)
    - HMG-CoA reductase inhibitors (e.g., simvastatin, lovastatin)
    - Other (e.g., St. John's Wort)

For more detailed drug interaction information, reference the most recent everolimus drug label[1].

Everolimus is approved in the United States under the name of Zortress‡ for the prophylaxis of organ rejection in adult kidney transplant recipients at low-moderate immunologic risk, at the dose of 1.5 mg / day when taken by mouth. Outside the United States, Zortress‡ is sold under the brand name Certican‡ in more than 70 countries. Everolimus is also approved in the United States and Europe under the name of Afinitor‡ for the treatment of patients with advanced renal cell carcinoma (cancer) after failure of treatment with sunitinib or sorafenib, at doses of 5 mg/day to 20 mg/day when taken by mouth. The amount of drug that circulates in the bloodstream following implantation of an Esprit BTK Scaffold is lower than that obtained with prolonged oral doses (1.5 mg/day to 20 mg/day).

6.12.2 Immune Suppression Potential

Everolimus, the Esprit BTK Scaffold's active pharmaceutical ingredient, is an immunosuppressive agent. Immune suppression was not observed in the LIFE-BTK clinical trial. However, for patients who receive several Esprit BTK Scaffolds simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

6.12.3 Lipid Elevation Potential

Oral everolimus use in renal transplant and advanced renal cell carcinoma patients was associated with increased serum cholesterol and triglyceride levels, which in some cases required treatment. The effect was seen with both low and high dose prolonged oral therapy in a dose-related manner.

Oral administration of everolimus in combination with cyclosporine has been associated with increased serum cholesterol and triglyceride levels.

When used according to the indications for use, exposure to systemic everolimus concentrations from the Esprit BTK Scaffold is expected to be lower than concentration exposure usually obtained in transplant patients.

[1] Certican‡ UK SmPC, Afinitor‡ UK SmPC, Votubia‡ UK SmPC, Afinitor‡ US label, and Zortress‡ US label. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SmPC / labels.

6.12.4 Pregnancy

Pregnancy Category C: There are no adequate everolimus or Esprit BTK Scaffold-related studies in pregnant women.

Effects on the developing fetus have not been studied[1]. Effects of a similar device (XIENCE V™ stent), on prenatal and postnatal rat development were no different than the controls (See *Section 6.13 Carcinogenicity, Genotoxicity, and Reproductive Toxicity*). When administered at oral doses of 0.1 mg/kg or above to animals, everolimus has shown reproductive toxicity effects including embryotoxicity and fetotoxicity.

Effective contraception is recommended to be initiated before implanting an Esprit BTK Scaffold and continued for one-year post-implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time[1].

6.12.5 Lactation

It is unknown whether everolimus is distributed in human milk. Everolimus pharmacokinetic and safety profiles have not been determined in infants. Consequently, mothers should be advised of potential serious adverse reactions to everolimus in nursing infants. Prior to Esprit BTK Scaffold implantation, decisions should be made regarding whether to discontinue nursing or conduct an alternate procedure.

6.13 Carcinogenicity, Genotoxicity, and Reproductive Toxicity

The carcinogenicity, genotoxicity, and reproductive toxicity of the Esprit BTK Scaffold have been evaluated with a conclusion of no carcinogenicity, genotoxicity or reproductive toxicity concerns. The evaluation is based on the following aspects:

- No Genotoxicity of Esprit BTK Scaffold:

  The Esprit BTK Scaffold is identical in scaffold material and drug to the Absorb GT1™ Bioresorbable Vascular Scaffold (BVS) (identical drug and polymers, drug:polymer formulation, drug dose density and drug coating process). Absorb GT1™ Scaffold passed genotoxicity studies. The test results are applicable to Esprit BTK Scaffold. The genotoxicity test (Ames) was performed on Esprit BTK Scaffold for confirmational purposes.

- No Carcinogenicity or Reproductive Toxicity of the Esprit BTK Scaffold:

  The Esprit BTK Scaffold is identical in scaffold material and drug to the Absorb GT1 scaffold. Absorb GT1 Scaffold has gone through chemical characterization and toxicological risk assessment. These evaluations concluded there are no concerns of the carcinogenicity or reproductive toxicity evaluated. The results are applicable to the Esprit BTK Scaffold. Furthermore, carcinogenicity and reproductive toxicity (teratology) studies conducted on the XIENCE V™, a similar everolimus-eluting coronary stent system, demonstrated no concerns on the drug (everolimus) for carcinogenicity and reproductive toxicity. The test results are also applicable to Esprit BTK Scaffold from the drug perspective.

[1] Certican‡ UK SmPC, Afinitor‡ UK SmPC, Votubia‡ UK SmPC, Afinitor‡ US label, and Zortress‡ US label. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SmPC / labels.

7.0 DRUG INFORMATION

7.1 Mechanism of Action

At the cellular level, everolimus inhibits growth factor-stimulated cell proliferation. At the molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12 (FK 506 Binding Protein). This complex binds to and interferes with FKBP-12 Rapamycin Associated Protein (FRAP), also known as mammalian target of rapamycin (mTOR), leading to inhibition of cell metabolism, growth, and proliferation by arresting the cell cycle at the late G1 stage.

7.2 Pharmacokinetics

The everolimus elution from the Esprit™ BTK Scaffold post-implantation has been evaluated in a pharmacokinetic (PK) sub-study, which is part of the LIFE-BTK clinical trial design studying the Esprit™ BTK System in the United States (US) and outside of the US. A total of 9 subjects who received only Esprit™ BTK Scaffold System at investigational sites in the US, Taiwan, and Australia were registered in the PK sub-study. All subjects had target lesions that were treated with only Esprit BTK System. The number of scaffolds implanted per subject ranged from 5 to 8. The total dose of everolimus received by the subjects ranged from 1397 to 2074 µg. *Table 7.2-1* provides whole blood everolimus PK parameters determined from the subjects receiving the Esprit BTK Scaffold.

Table 7.2-1: Pharmacokinetic Results of Everolimus after Implantation of Esprit BTK Scaffold

Pharmacokinetics of Everolimus	LIFE-BTK PK Sub-Study
Number of subjects	9
Number of scaffolds used per subject - range	5-8
Total dose received (µg)	1397-2074
C_{max} range (ng/mL)	9.6-50.5
AUC_t range (ng·h/mL)	243-1100
Median t_{max} (h)	0.25
$t_{1/2}$ range (h)	65.6-211.2

Note: Ranges are provided for dose, C_{max}, AUC_t, and $t_{1/2}$, and median for t_{max}.
C_{max} = maximum observed blood concentration
AUC_t = the area beneath the blood concentration versus time curve: time zero to the final quantifiable concentration
t_{max} = time to maximum concentration
$t_{1/2}$ = terminal phase half-life

Everolimus blood concentrations were low (C_{max} range from 9.6 - 50.5 ng/ml) and could be quantified only up to 720 hours (h) after implantation of the last Esprit BTK Scaffold. These C_{max} values are lower than those in transplant or oncology patients. In addition, compared to the prolonged exposure in transplant or oncology patients (weeks to months), the single exposure in subjects with the Esprit BTK Scaffold leads to a transient increase and rapid disappearance of everolimus, which further limits the systemic extent of exposure. Therefore, everolimus blood concentrations seen with the Esprit BTK Scaffold are considered safe.

The pharmacokinetic profile for everolimus eluted from the Esprit BTK Scaffold has been characterized and is consistent with previous clinical and nonclinical data, including that from previous Abbott studies on a similar device Absorb GT1 scaffold (ABSORB III RCT).

In the treatment of infrapopliteal lesions in the PK sub-study, subjects received 180 – 256 mm in scaffold length or a dose of 1397-2074 µg everolimus. The PK parameters based on the LIFE-BTK PK sub-study data suggest that at the dose range tested, the drug concentration drops below detectable levels at up to 720 hours after the last scaffold implantation. The rapid disappearance of everolimus from the systemic circulation after Esprit BTK Scaffold implantation limits the total systemic exposure of subjects to the drug. Based on the pharmacokinetic profiles seen with the Esprit BTK Scaffold in this study, the usage in infrapopliteal lesions is considered to be safe.

7.3 Interactions with Drugs or Other Substances

For information on interactions with drugs or other substances, see *Section 6.12.1 Interactions with Drugs or Other Substance*.

8.0 ADVERSE EVENTS

8.1 Observed Adverse Events

Adverse events observed in the Esprit™ BTK System clinical trial that are related to the key clinical outcomes of death, MALE (Major Adverse Limb Events: major amputation or major re-interventions including new bypass graft, jump / interposition graft revision, or thrombectomy / thrombolysis related to the target lesion), target vessel occlusion, target lesion restenosis, target vessel and target lesion revascularization are presented in *Section 9.0 Clinical Investigations of the Esprit BTK System*. All other adverse events are included in *Section 8.2 Potential Adverse Events*.

8.2 Potential Adverse Events

Potential adverse events include, but are not limited to:

Allergic reaction or hypersensitivity to contrast agent, anesthesia, scaffold materials (poly[L-lactide] [PLLA], poly[D, L-lactide] [PDLLA], platinum, or everolimus), and drug reactions to anticoagulation or antiplatelet drugs

- Vascular access complications which may require transfusion or vessel repair, including:
  - Catheter site reactions
  - Bleeding (ecchymosis, oozing, hematoma, hemorrhage, retroperitoneal hemorrhage)
  - Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture, and laceration
  - Embolism (air, tissue, plaque, thrombotic material, or device)
  - Peripheral ischemia

- Target artery complications which may require additional intervention, including:
  - Total occlusion or abrupt closure
  - Arteriovenous fistula, pseudoaneurysm, aneurysm, dissection, perforation / rupture
  - Embolism (air, tissue, plaque, thrombotic material, or device)
  - Artery or scaffold thrombosis
  - Stenosis or restenosis
  - Vasospasm
  - Tissue prolapse / plaque shift
- Bleeding (non-access site)
- Additional surgery such as peripheral artery bypass graft surgery or amputation
- Peripheral nerve injury, neuropathy
- Compartment syndrome
- Tissue necrosis, gangrene, ulcer and acute limb ischemia
- Reperfusion injury
- New or worsening pain
- Intervention due to
  - Damaged scaffolds
  - Partial scaffold deployment
  - Scaffold migration / unintentional placement of scaffold
- Other general surgical risks, including:
  - Cardiac arrhythmias (including conduction disorders, atrial and ventricular arrhythmias, and blocks)
  - Stroke / cerebrovascular accident (CVA) and transient ischemic attack (TIA)
  - Venous thromboembolism (including pulmonary embolism)
  - Nausea and vomiting
  - Hypotension / hypertension
  - Infection – local and systemic (including post-procedural)
  - Fever
  - Blood cell disorders including heparin-induced thrombocytopenia (HIT) and other coagulopathy
  - Death
- System organ failures:
  - Cardiac failure
  - Cardio-respiratory arrest (including pulmonary edema)
  - Respiratory failure
  - Renal failure
  - Shock

Adverse events associated with daily oral administration of everolimus in doses varying from 1.5 mg to 10 mg daily can be found in the Summary of Product Characteristics (SmPC) and labels for the drug[1]. The risks described below include the anticipated adverse events referenced in the contraindications, warnings, and precautions sections of the everolimus labels / SmPCs and / or observed at incidences ≥ 10% in clinical trials with oral everolimus for different indications. Refer to the drug SmPCs and labels for more detailed information and less frequent adverse events.

- Abdominal pain
- Anemia
- Angioedema (increased risk with concomitant angiotensin-converting enzyme [ACE] inhibitor use)
- Arterial thrombotic events
- Bleeding and coagulopathy (including hemolytic uremic syndrome [HUS], thrombotic thrombocytopenic purpura [TTP], and thrombotic microangiopathy; increased risk with concomitant cyclosporine use)
- Constipation
- Cough
- Diabetes mellitus
- Diarrhea
- Dyspnea
- Embryo-fetal toxicity
- Erythema
- Erythroderma
- Headache
- Hepatic artery thrombosis (HAT)
- Hepatic disorders (including hepatitis and jaundice)
- Hypersensitivity to everolimus active substance, or to other rapamycin derivates
- Hypertension
- Infections (bacterial, viral, fungal, or protozoan infections, including infections with opportunistic pathogens). Polyoma virus-associated nephropathy (PVAN), JC virus-associated progressive multiple leukoencephalopathy (PML), fatal infections and sepsis have been reported in patients treated with oral everolimus.
- Kidney arterial and venous thrombosis
- Laboratory test alterations (elevations of serum creatinine, proteinuria, hypokalemia, hyperkalemia; hyperglycemia, dyslipidemia including hypercholesterolemia and hypertriglyceridemia; abnormal liver function tests; decreases in hemoglobin, lymphocytes, neutrophils, and platelets)
- Lymphoma and skin cancer
- Male infertility
- Menstrual irregularities

[1] Certican‡ UK SmPC, Afinitor‡ UK SmPC, Votubia‡ UK SmPC, Afinitor‡ US label, and Zortress‡ US label. Refer to www.MHRA.gov.uk, www.ema.europa.eu, and www.fda.gov for the most recent versions of these SmPC / labels.

- Nausea
- Nephrotoxicity (in combination with cyclosporine)
- Non-infectious pneumonitis (including interstitial lung disease)
- Oral ulcerations
- Pain
- Pancreatitis
- Pericardial effusion
- Peripheral edema
- Pleural effusion
- Pneumonia
- Pyrexia
- Rash
- Renal failure
- Upper respiratory tract infection
- Urinary tract infection
- Venous thromboembolism
- Vomiting
- Wound healing complications (including wound infections and lymphocele)

There may be other potential adverse events that are unforeseen at this time.

9.0 CLINICAL INVESTIGATIONS OF THE Esprit™ BTK SYSTEM

The safety and effectiveness of the Esprit BTK System is supported with data from the pivotaL Investigation of saFety and Efficacy of BRS[2] treatment-Below The Knee (LIFE-BTK) clinical investigation.

LIFE-BTK consists of a randomized cohort (described below) and a non-randomized Pharmacokinetics (PK) sub-study. Results from the PK sub-study are presented in *Section 7.2 Pharmacokinetics*. Enrollment in LIFE-BTK has been completed, and all subjects are past 1-year post-index procedure. Clinical follow-up through 5 years is ongoing.

[2] BRS: BioResorbable Scaffold.

9.1 LIFE-BTK Randomized Controlled Trial (RCT)

9.1.1 Primary Objective

LIFE-BTK RCT was designed to evaluate the safety and effectiveness of the everolimus eluting Esprit BTK System for the planned treatment of narrowed infrapopliteal lesions.

9.1.2 Design

LIFE-BTK RCT is a prospective, single-blinded, randomized controlled clinical study. A total of 261 subjects were randomized between Esprit BTK therapy and PTA therapy (173 subjects in the Esprit BTK arm and 88 subjects in the PTA arm). Subjects were randomized in a 2:1 ratio (Esprit BTK: PTA). The clinical investigation was conducted at 50 clinical sites across 6 countries that included the US, Singapore, Hong Kong, Taiwan, Australia, and New Zealand.

Eligible subjects were 18 years or older and consented to participate in the study. Chronic limb-threatening ischemia (CLTI) subjects with Rutherford Becker class 4 or 5 who had arterial narrowing in infrapopliteal lesions with ≥ 70% stenosis and diameters of 2.5 – 4.0 mm using visual angiographic assessment were eligible to enroll. Restenotic (from prior PTA) infrapopliteal lesions were allowed, but in-stent restenosis was an exclusion. LIFE-BTK RCT allowed up to a total of 170 mm length of Esprit™ BTK Scaffolds to be implanted per subject. Subject randomization occurred after all eligibility criteria were met, all in-flow and non-target lesion(s) had been treated successfully, and the guide wire had successfully crossed the target lesion. In the Esprit BTK arm, pre-dilatation of the target lesion was mandatory. Successful pre-dilatation was defined as residual diameter stenosis of < 30%. After successful pre-dilatation and vessel sizing of the target lesion, the final scaffold diameter was chosen by using the pre-dilatation balloon size as a guide. The maximum total scaffolded length of 170 mm per subject could be in a single target lesion or divided across 2 target lesions. Coverage of the entire length of the pre-dilated segment with the implanted scaffold(s) was mandated. Post-dilatation of the scaffold was required for all treated lesions. For the PTA arm, the treatment was done per standard of care. Technical success was defined on a per lesion basis as the attainment of a final residual stenosis of < 30% at the intended target lesion(s) following use of the study device(s). Standard pre-dilatation catheters and post-dilatation catheters (if applicable) were allowed to be used. Bailout at lesion level did not impact technical success if the above criteria were met.

Subject clinical follow-up occurred at 30 days, 3 months, 6 months, and 1 year, and will be continued annually to complete 5 years of follow-up. Duplex ultrasound was conducted at 30 days, 180 days, 1 year, and will be conducted at 2 years and 3 years. Follow-up visits are conducted at the site. To aid in follow-up compliance, follow-up visits may also be conducted in-home using the third-party service provided by the sponsor.

The two primary endpoints were as follows:

- The primary effectiveness endpoint was a composite of limb salvage and primary patency at 1 year. It included freedom from: above ankle amputation in the index limb, 100% total occlusion of the target vessel, binary restenosis of the target lesion, and clinically-driven target lesion revascularization (CD-TLR).

- The primary safety endpoint was freedom from MALE+POD (Major Adverse Limb Event + Peri-Operative Death). MALE included above ankle amputation in the index limb, major re-intervention on the index limb at 6 months and POD included perioperative mortality at 30 days.

The primary safety endpoint and primary effectiveness endpoint were evaluated when all subjects had completed their 1-year visit. The primary safety endpoint was based on the as-treated population and tested for non-inferiority of Esprit BTK to PTA. The primary effectiveness endpoint was based on the intent-to-treat population and tested for the superiority of Esprit BTK as compared to PTA.

The two powered secondary endpoints analyzed at 12 months were:

- Binary restenosis of the target lesion
- A composite endpoint of freedom from above ankle amputation of the index limb,100% total occlusion of the target vessel and CD-TLR.

Core laboratories were used for angiography, duplex ultrasound, intravascular ultrasound (IVUS), optical coherence tomography (OCT) and wound assessment. Adverse events were adjudicated by a clinical events committee (CEC) and a Data and Safety Monitoring Board (DSMB) reviewed cumulative data from the clinical investigation at regular intervals.

9.1.3 Demographics

Table 9.1.3-1 provides a summary of the baseline demographics and medical history of the 261 subjects randomized into the LIFE-BTK RCT study which included 88 subjects in the PTA group and 173 in the Esprit BTK group. The demographic and medical history of the subjects in the study were well balanced with no statistical differences between arms.

The mean ages were 73.3 ±9.9 and 71.1 ±10.4 years in the Esprit BTK and PTA arms, respectively. Over one-third of subjects in both arms were female. Out of the total registered population, 59% were identified as white and 41% as non-white, with 16.5% of the total population identified as Hispanic ethnicity. Mean body mass index values were 27.85 ±5.47 and 28.94 ±5.77 kg/m^2, in the Esprit BTK and PTA arms, respectively. Rutherford Becker (RB) Category in both arms was about evenly split between RB 4 and RB 5 and, hence, half of the population in both arms had wound(s) on the index limb at baseline.

Risk factors had a high prevalence in both arms, including diabetes (~70%), hypertension (90-95%), and hyperlipidemia (~80%). About half of the subjects in both arms were tobacco users, one-third of the population had previous percutaneous or surgical coronary revascularization, and about 60% in both arms had multi-vessel peripheral vascular disease. There were no significant differences between the Esprit BTK and PTA arms in baseline characteristics.

Table 9.1.3-1: Baseline Demographics and Medical History, Intent-to-Treat (N = 261)

	Esprit BTK (N = 173)	PTA (N = 88)
DEMOGRAPHICS		
Age (Year)		
Mean ±Standard Deviation (SD) (n)	73.3 ±9.9 (173)	71.1 ±10.4 (88)
Range (min, max)	(47, 94)	(49, 92)
Gender		
Male	67.6% (117/173)	69.3% (61/88)
Female	32.4% (56/173)	30.7% (27/88)
Race		
White	56.6% (98/173)	63.6% (56/88)
American Indian or Alaska Native	0.0% (0/173)	1.1% (1/88)
Asian	20.8% (36/173)	12.5% (11/88)
Chinese	77.8% (28/36)	100.0% (11/11)
South Asian	16.7% (6/36)	0.0% (0/11)
Other	5.6% (2/36)	0.0% (0/11)
Black or African American	12.1% (21/173)	12.5% (11/88)
Native Hawaiian or Other Pacific Islander	0.6% (1/173)	2.3% (2/88)
Declined or Unable to Disclose	10.4% (18/173)	8.0% (7/88)
Ethnicity		
Hispanic or Latino	17.9% (31/173)	13.6% (12/88)
Not Hispanic or Latino	76.3% (132/173)	79.5% (70/88)
Declined or Unable to Disclose	5.8% (10/173)	6.8% (6/88)
BMI		
Mean ±SD (n)	27.85 ±5.47 (173)	28.94 ±5.77 (88)
Range (min, max)	(18.0, 49.6)	(18.6, 45.9)
RISK FACTORS		
Tobacco Use	52.6% (91/173)	53.4% (47/88)
Hypertension	94.2% (163/173)	90.9% (80/88)
Hyperlipidemia	80.9% (140/173)	81.8% (72/88)
Diabetes Mellitus	71.1% (123/173)	69.3% (61/88)
MEDICAL HISTORY and PRESENTATION		
History of Peripheral Artery Disease	82.7% (143/173)	77.3% (68/88)
Multi-vessel Peripheral Vascular Disease	62.5% (105/168)	61.2% (52/85)
Previous Amputation to Target Limb	9.2% (16/173)	8.0% (7/88)
Cardiac History		
Prior Myocardial Infarction	16.9% (27/160)	14.8% (13/88)
Previous Percutaneous or Surgical Coronary Revascularization	34.7% (59/170)	35.6% (31/87)
Congestive Heart Failure	19.4% (33/170)	19.3% (17/88)

	Esprit BTK (N = 173)	PTA (N = 88)
Neurologic and Renal History		
Cerebrovascular Disease	13.2% (22/167)	17.4% (15/86)
Prior Cerebrovascular Accident (CVA) or Stroke	11.7% (20/171)	17.0% (15/88)
Transient Ischemic Attack	3.5% (6/170)	2.3% (2/87)
Renal Disease	15.8% (27/171)	16.3% (14/86)
Rutherford Becker Category		
RB4	52.0% (90/173)	51.1% (45/88)
RB5	48.0% (83/173)	48.9% (43/88)
ABI of Target Limb		
Mean ±SD (n)	0.87 ±0.32 (150)	0.91 ±0.33 (77)
TBI of Target Limb		
Mean ±SD (n)	0.51 ±0.31 (50)	0.46 ±0.24 (29)
Wound on Target Limb at baseline	49.1% (85/173)	51.1% (45/88)

N: Total number of subjects.
n: Number of subjects with available data for variable of interest.
Data presented as % (n/N) or Mean ±standard deviation.
BMI: Body Mass Index; ABI: Ankle Brachial Index; TBI: Toe Brachial Index

Table 9.1.3-2 presents the baseline, procedure, and post-procedure target lesion characteristics by the angiographic core laboratory. There was a total of 179 target lesions in 173 subjects in the Esprit BTK arm, and 92 target lesions in 88 subjects in the PTA arm. The majority of the target lesions segment was located in the anterior tibial, with 34.3% (59/172) and 27.0% (24/89) in the Esprit BTK arm and PTA arm, respectively. The mean lesion length (~44 mm) and mean reference vessel diameter (~2.9 mm) were similar between the arms. The mean pre-procedure percentage of diameter stenosis (%DS) was 72.6 ±18.9% in the Esprit BTK arm and 73.7 ±21.0% in the PTA arm. At post-procedure, the mean in-device and in-segment %DS were numerically lower in the Esprit BTK arm compared to the PTA arm. The Esprit BTK arm also achieved a higher percentage of final diameter %DS < 30% at the rate of 95.9% (163/170) compared to the PTA arm which had a rate of 72.6% (61/84).

Table 9.1.3-2: Baseline, Procedure and Post-Procedure Target Lesion Characteristics, Intent-to-Treat (N = 261)

	Esprit BTK (N = 173) (L = 179)	PTA (N = 88) (L = 92)
Baseline Angiographic Core Laboratory Reported Lesion Characteristics		
Artery Segment		
Anterior Tibial	34.3% (59/172)	27.0% (24/89)
Posterior Tibial	15.1% (26/172)	18.0% (16/89)
Peroneal	16.3% (28/172)	23.6% (21/89)
Tibioperoneal Trunk	15.1% (26/172)	16.9% (15/89)
Tibioperoneal Trunk – Posterior Tibial	8.7% (15/172)	9.0% (8/89)
Tibioperoneal Trunk – Peroneal	10.5% (18/172)	5.6% (5/89)
Lesion Length (mm)		
Mean ±SD (l)	43.78 ±31.84 (172)	44.75 ±29.07 (89)
Range (min, max)	(3.82, 148.40)	(5.33, 125.10)
Reference Vessel Diameter Pre-intervention		
Mean ±SD (l)	2.94 ±0.77 (147)	2.82 ±0.74 (80)
Range (min, max)	(1.37, 5.23)	(1.35, 4.79)
Calcification		
None	99.4% (171/172)	100.0% (89/89)
Moderate	0.6% (1/172)	0.0% (0/89)
Thrombus		
Absent	100.0% (172/172)	100.0% (89/89)
Ulceration	0.0% (0/172)	0.0% (0/89)
Aneurysm	0.0% (0/172)	0.0% (0/89)
TASC II Type		
A	48.3% (83/172)	52.8% (47/89)
B	35.5% (61/172)	25.8% (23/89)
C	16.3% (28/172)	21.3% (19/89)
D	0.0% (0/172)	0.0% (0/89)
% Diameter Stenosis (DS) Pre-intervention		
Mean ±SD (l)	72.6 ±18.9 (172)	73.7 ±21.0 (89)
Range (min, max)	(23, 100)	(18, 100)
Total Occlusion at Treatment Site	15.1% (26/172)	20.2% (18/89)
Angiographic Core Laboratory Reported Post-Procedure Measurements		
Residual %DS after Pre-dilatation/PTA		
Mean ±SD (l)	30.0 ±12.6 (84)	25.0 ±8.7 (3)
Range (min, max)	(3, 61)	(15, 31)
Post-procedure In-Device %DS		
Mean ±SD (l)	13.1 ±8.2 (170)	21.8 ±11.4 (84)
Range (min, max)	(-9, 35)	(-7, 48)
Post-procedure In-Segment %DS		
Mean ±SD (l)	17.0 ±9.3 (170)	22.8 ±11.2 (84)
Range (min, max)	(-6, 60)	(-5, 48)
Final Diameter Stenosis < 30%	95.9% (163/170)	72.6% (61/84)
Residual Dissection Post-Intervention	0.0% (0/170)	0.0% (0/84)
Procedural Characteristics (Site-Reported)		
Pre-dilation Performed	100.0% (179/179)	100.0% (92/92)
Scaffold Post-dilated Without Complications	99.4% (176/177)	NA
Metal Stent Bailout	0.0% (0/173)	5.7% (5/88)

N: Number of subjects. L: Total number of target lesions. l: Number of target lesions with available data for variable of interest
TASC II: Trans-Atlantic Inter-Society Consensus.
NA: Not applicable.
Data presented as %(l/L) or Mean ±standard deviation.

Table 9.1.3-3 presents an overview of scaffold usage in subjects from the Esprit BTK arm. A total of 339 scaffolds (S) were implanted in 179 lesions (L). The most frequent scaffold diameter used was 3.0 mm, and the most frequent scaffold length used was 38 mm. The mean total number of scaffolds implanted per subject was 2.0 ±1.3, and the mean total scaffold length per subject was 63.6 ±47.0 mm.

Table 9.1.3-3: Esprit BTK Scaffold Usage, Intent-to-Treat (N = 261)

	Esprit BTK (N = 173) (L = 179) (S = 339)
Scaffold diameters used %(s/S)	
2.5 mm	18.3% (62/339)
3.0 mm	45.7% (155/339)
3.5 mm	27.7% (94/339)
3.75 mm*	8.3% (28/339)
Scaffold length used %(s/S)	
18 mm	18.3% (62/339)
28 mm	24.5% (83/339)
38 mm	57.2% (194/339)
Total number of scaffolds implanted per lesion	
Mean ±SD (l)	1.9 ±1.3 (176)
Range (min, max)	(1, 6)
1 scaffold per lesion	52.8% (93/176)
2 scaffolds per lesion	22.7% (40/176)
3 scaffolds per lesion	12.5% (22/176)
4 scaffolds per lesion	5.1% (9/176)
5 scaffolds per lesion	4.5% (8/176)
6 scaffolds per lesion	2.3% (4/176)
Total number of scaffolds implanted per subject	
Mean ±SD (n)	2.0 ±1.3 (170)
Range (min, max)	(1, 6)
1 scaffold per subject	50.6% (86/170)
2 scaffolds per subject	23.5% (40/170)
3 scaffolds per subject	12.4% (21/170)
4 scaffolds per subject	5.9% (10/170)
5 scaffolds per subject	4.7% (8/170)
6 scaffolds per subject	2.9% (5/170)
Total scaffold length per lesion (mm)	
Mean ±SD (l)	61.4 ±45.5 (176)
Range (min. max)	(18, 190)
Total scaffold length per subject (mm)	
Mean ±SD (n)	63.6 ±47.0 (170)
Range (min. max)	(18, 190)

N: Total number of subjects. n: Number of subjects with available data for variable of interest. L: Total number of target lesions. l: Number of target lesions with available data for variable of interest. s: Number of scaffolds with available data for variable of interest. S: number of scaffolds implanted.
Data presented as %(s/S) or Mean ±standard deviation.

*The 3.75 mm scaffold sizes were introduced in the trial when approximately 50 subjects (out of 261) had already been enrolled.

9.1.4 Results

9.1.4.1 Primary Safety and Effectiveness Endpoints

Results for the primary safety and effectiveness endpoints of the LIFE-BTK RCT are described and summarized in *Table 9.1.4.1-1*, and *Figures 9.1.4.1-1* and *9.1.4.1-2*.

Both the primary safety and primary effectiveness endpoints were met.

In the as-treated (AT) population, the Esprit BTK arm was non-inferior to PTA arm, the primary safety endpoint was met (p-value = 0.0019).

Based on the intent-to-treat (ITT) population, the composite effectiveness rate at 1 year was 43.7% (31/71) in the PTA arm and 74.5% (111/149) in the Esprit BTK arm with a difference between the two treatment arms of 30.8%. The Esprit BTK arm was superior to PTA, with a superiority p-value of < 0.0001, for device effectiveness.

Table 9.1.4.1-1 Primary Safety and Effectiveness Endpoints

Primary Safety Endpoint				
As-Treated (N = 260)	**Esprit BTK (N = 170)**	**PTA (N = 90)**	**Difference (One Sided Lower 97.5% CL)[2]**	**Non-inferiority P-value[3]**
Freedom from MALE[1] at 6 months and POD at 30 days	96.9% (155/160)	100.0% (85/85)	-3.13% (-7.11%)	0.0019
Primary Effectiveness Endpoint				
Intent-to-Treat (N = 261)	**Esprit BTK (N = 173)**	**PTA (N = 88)**	**Difference (One Sided Lower 97.51% CL)[2]**	**Superiority P-value[5]**
Limb Salvage and Primary Patency at 1 year[4]	74.5% (111/149)	43.7% (31/71)	30.83% (17.01%)	< 0.0001

[1] For the MALE component, the adverse event start date is used as the treatment date.

[2] By Newcombe score method.

[3] Farrington-Manning non-inferiority NI) test, with NI margin of δ set at -10%, to be compared at one-sided significance level of 0.025.

Note: MALE includes above ankle amputation in index limb, major re-intervention on index limb at 6 months and POD includes perioperative mortality at 30 days.

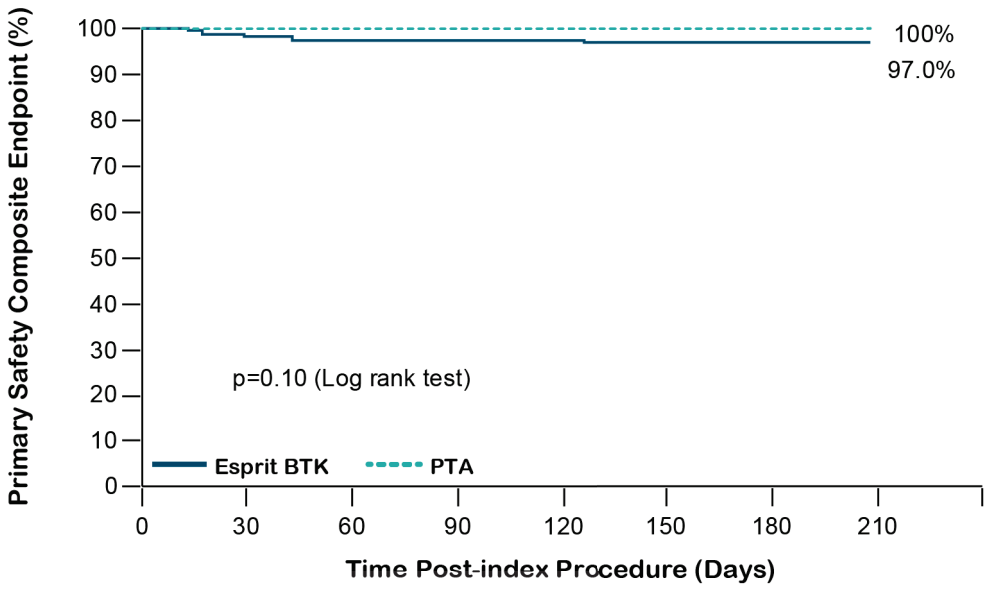
[4] Composite of Limb Salvage and Primary Patency includes freedom from: above ankle amputation in index limb, 100% total occlusion of target vessel, binary restenosis of target lesion, and CD-TLR. For the amputation and CD-TLR components, the adverse event start date is used as the treatment date.

[5] From One-sided Chi-square test, to be compared at one-sided significance level of 0.0249. The final alpha level of 0.0249 was adjusted down from the nominal 0.025 due to a pre-specified interim look by an independent statistician for sample size re-estimation.

N: Total number of subjects.

CL: Confidence level.

The Kaplan-Meier curve showing the composite rates of freedom from MALE + POD through 6 months post-index procedure is presented below.



Time After Index Procedure (days)						
	0	**30**	**60**	**90**	**180**	**208**
Esprit BTK:						
# At Risk	170	166	162	162	153	152
% Survived	100.0%	98.2%	97.6%	97.6%	97.0%	97.0%
PTA:						
# At Risk	90	90	89	87	84	84
% Survived	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

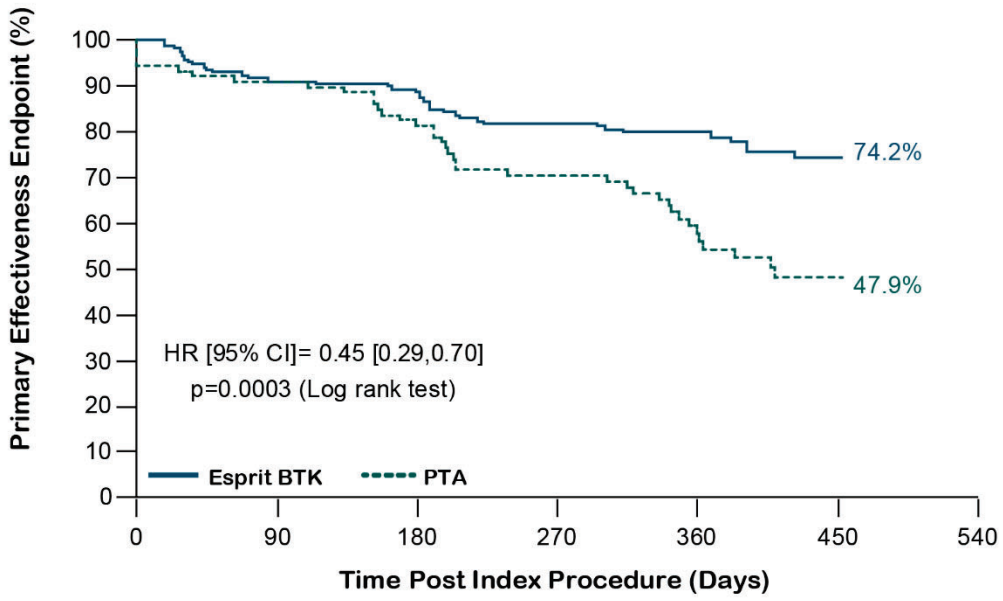
Test Between Groups	**Test**	**Chi-Square**	**Degree of Freedom (DF)**	**p-value**
	Log-Rank	2.684	1	0.10

Note: Data are presented as the event-free rates (binary) through 6 months (208 days post-index procedure) for the Major Adverse Limb Event by CEC adjudication, and through 30 days post-index procedure for the Peri-operative Death by CEC adjudication.
Note: Events include only each subject's first occurrence of the composite endpoint.
Note: The p-value presented here was not adjusted for multiplicity.

Figure 9.1.4.1-1: Kaplan-Meier Survival Curve: Primary Safety Endpoint (Freedom from MALE + POD) by Treatment through 6 Months (As-Treated Population)

The Kaplan-Meier curve (KM curve) showing the composite rates of primary patency and limb salvage from index procedure through 1 year in the intent-to-treat population is shown below.

Two of the primary effectiveness endpoint components (100% total occlusion of target vessel and binary restenosis of target lesion) were dependent on imaging, mainly duplex ultrasound (DUS). DUS exams that were non-diagnostic (i.e., not analyzable by the core laboratory) were asked to be repeated. The 1-year window was extended to 453 days to allow for these repeat DUS exams to occur and ensure a totality of DUS data collection. Therefore, the KM curve below extends to 453 days.



Time After Index Procedure (days)						
	0	**30**	**90**	**180**	**365**	**453**
Esprit BTK:						
# At Risk	173	163	152	142	95	42
% Survived	100.0%	96.5%	91.1%	88.6%	79.8%	74.2%
PTA:						
# At Risk	88	82	78	67	33	15
% Survived	94.3%	93.2%	90.9%	81.2%	54.5%	47.9%

Test Between Groups	**Test**	**Chi-Square**	**DF**	**p-value**
	Log-Rank	13.104	1	0.0003

Note: Data are presented as the event-free rates through 1-year post index procedure.
Note: Events include only each subject's first occurrence of the composite endpoint.
Note: The p-value and the 95% CI were calculated without multiplicity adjustment.

Figure 9.1.4.1-2: Kaplan-Meier Survival Curve: Primary Effectiveness Endpoint by Treatment through 1 Year (Intent-to-Treat Population)

9.1.4.2 Powered Secondary Endpoints

The first powered secondary endpoint, binary restenosis of target lesion at 1 year, and the second powered secondary endpoint, a composite of freedom from: above ankle amputation in index limb, 100% total occlusion of target vessel and CD-TLR, are shown in *Table 9.1.4.2-1*.

Both powered secondary endpoints were met showing superiority of Esprit BTK over PTA. The binary restenosis rates were 23.5% (35/149) for the Esprit BTK arm and 49.3% (35/71) for the PTA arm with a difference of -25.8%, with a p-value of < 0.0001. The second powered secondary endpoint rates were 83.2% (124/149) for the Esprit BTK arm and 69.0% (49/71) for the PTA arm with a difference of 14.2%, with a p-value of 0.0081.

Table 9.1.4.2-1: Powered Secondary Endpoints, Intent-to-Treat (N = 261)

First Powered Secondary Endpoint: Binary Restenosis of Target Lesion at 1 year				
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Difference (One Sided Upper 97.5% CL)[1]**	**Superiority P-value[2]**
Binary Restenosis of the Target Lesion at 1 year[3]	23.5% (35/149)	49.3% (35/71)	-25.81% (-12.30%)	< 0.0001
Second Powered Secondary Endpoint: Limb Salvage and Primary Patency at 1 year: Freedom From Above Ankle Amputation in Index Limb, 100% Total Occlusion of Target Vessel, and CD-TLR				
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Difference (One Sided Lower 97.5% CL)[1]**	**Superiority P-value[2]**
Limb Salvage and Primary Patency at 1 year (without binary restenosis)[4]	83.2% (124/149)	69.0% (49/71)	14.21% (2.48%)	0.0081

[1] By Newcombe score method.

[2] From One-sided Chi-square test, to be compared at one-sided significance level of 0.025.

[3] Binary restenosis is defined as the presence of a hemodynamically significant restenosis > 50% by angiography, or PSVR ≥ 2.0 by duplex ultrasound. In the presence of abnormal reference PSV, the DUS core laboratory used the following additional secondary criteria (correlating factors) to identify target lesion stenoses > 50% in severity: 1) Focal increase in the absolute PSV at the area of visible plaque; 2) Spectral broadening of the waveform at the area of stenosis; 3) Post-stenotic turbulence (PST) and/or change in the waveform shape and/or drop in velocity distal to the stenosis; 4) Review of the B-mode images for plaque burden.

[4] For the amputation and CD-TLR components, the adverse event start date is used as the treatment date.

N: Total number of subjects. Limb salvage and primary patency is defined as freedom from: above ankle amputation in index limb, 100% total occlusion of target vessel, and clinically-driven target lesion revascularization (CD-TLR).

9.1.4.3 Principal Safety and Effectiveness Results

Procedural outcomes are presented in *Table 9.1.4.3-1*. The rate of technical success was significantly higher for the Esprit BTK arm compared to the PTA arm. It should be noted that there were specific protocol requirements for the implantation of Esprit BTK (see *Section 9.1.2 Design*), whereas the PTA procedure was performed per standard of care.

Non-hierarchical components for the primary safety and effectiveness endpoints are presented in *Table 9.1.4.3-2*. Other key descriptive endpoints are also presented in this table.

As presented in *Section 9.1.4.1 Primary Safety and Effectiveness Endpoints*, the primary safety endpoint was met and the Esprit BTK arm is concluded to be non-inferior to the PTA arm for device safety. For each of the components, MALE and POD, there were no significant difference between the Esprit BTK arm and the PTA arm.

For the primary effectiveness endpoint, the components of Freedom from 100% Total Occlusion of the Target Vessel, Freedom from Binary Restenosis of the Target Lesion, and Freedom from CD-TLR were all numerically higher in the Esprit BTK arm as compared to the PTA arm. Major amputation event rates were low in each arm and statistically not different.

There were 4 above-ankle amputations in the Esprit BTK arm, two within the first 6 months and two between 6 months and 1 year. All were determined to be not related to or unlikely to be related to the study device. All 4 subjects with amputation had diabetes and presented with index wounds. Three subjects had patent scaffolds at the time of amputation. The fourth subject had a site-reported duplex ultrasound suggesting scaffold occlusion which at follow-up was found to be patent on angiography.

Table 9.1.4.3-1: Procedural Endpoints

	Esprit BTK (N = 173) (L = 179) (D = 356)	**PTA (N = 88) (L = 92)**	**Difference [95% CI][1]**
Technical Success	95.9% (163/170)	72.6% (61/84)	23.26% [13.91%, 33.84%]
Device Success	95.2% (339/356)	NA	NA

[1] By Newcombe score method. The confidence interval was calculated without any multiplicity adjustment.

N: Total number of subjects. L: Number of target lesions. D: Number of devices. NA: Not applicable.

Technical Success is defined on a per lesion basis as the attainment of a final residual stenosis of < 30% at the intended target lesion(s) following use of the study device(s). Standard pre-dilatation catheters and post-dilatation catheters (if applicable) may be used. Bailout at lesion level does not impact technical success if the above criteria are met. Measurements of % diameter stenosis for technical success were per angiographic core laboratory.

Device success is defined on a per device basis, as the achievement of successful delivery and deployment of the study device(s) at the intended target lesion and successful withdrawal of the delivery catheter.

Table 9.1.4.3-2: Principal Safety and Effectiveness Results

Primary Safety Endpoint and Components – As-Treated (N = 260)			
	Esprit BTK (N = 170)	**PTA (N = 90)**	**Difference [95% CI][1]**
Primary Safety Endpoint Freedom from MALE[2] at 6 months and POD at 30 days	96.9% (155/160)	100.0% (85/85)	-3.13% [-7.11%, 1.55%]
Freedom from Major Adverse Limb Events[2] at 6 months	98.1% (157/160)	100.0% (85/85)	-1.88% [-5.37%, 2.62%]
Freedom from Above Ankle Amputation in Index Limb	98.8% (158/160)	100.0% (85/85)	-1.25% [-4.44%, 3.17%]
Freedom from Major Re-intervention on Index Limb	99.4% (159/160)	100.0% (85/85)	-0.63% [-3.45%, 3.73%]
Freedom from Peri-Operative Death (POD) at 30 days	98.8% (158/160)	100.0% (85/85)	-1.25% [-4.44%, 3.17%]
Primary Effectiveness Endpoint and Components – Intent-to-Treat (N = 261)			
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Difference [95% CI][1]**
Primary Effectiveness Endpoint at 1 year Limb Salvage and Primary Patency	74.5% (111/149)	43.7% (31/71)	30.83% [17.02%, 43.45%]
Freedom from Above Ankle Amputation in Index Limb[3]	97.3% (145/149)	100.0% (71/71)	-2.68% [-6.70%, 2.70%]
Freedom from 100% Total Occlusion of Target Vessel	87.9% (131/149)	83.1% (59/71)	4.82% [-4.50%, 16.04%]
Freedom from Binary Restenosis of the Target Lesion	76.5% (114/149)	50.7% (36/71)	25.81% [12.30%, 38.70%]
Freedom from CD-TLR[3]	92.6% (138/149)	84.5% (60/71)	8.11% [-0.40%, 18.76%]
Other Key Effectiveness Results – Intent-to-Treat (N = 261)			
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Difference [95% CI][1]**
CD-TLR within 1 year[3]	6.5% (11/170)	12.8% (11/86)	-6.32% [-15.44%, 0.94%]
Clinically driven Target Vessel Revascularization at 1-year[3]	6.5% (11/170)	15.1% (13/86)	-8.65% [-18.12%, -0.95%]
Acute and Subacute Thrombosis[4] (0 – 30 days) at the Target Lesion	0.0% (0/169)	0.0% (0/88)	0.00% [-4.18%, 2.22%]
Late Thrombosis[4] (31 – 365 days) at the Target Lesion	0.0% (0/154)	0.0% (0/81)	0.00% [-4.53%, 2.43%]

[1] By Newcombe score method.

[2] For the MALE component, the adverse event start date is used as the treatment date.

[3] For the amputation, CD-TLR, and Clinically-Driven Target Vessel Revascularization components, the adverse event start date is used as the treatment date.

[4] Thrombosis data is based on angiographic core laboratory assessment.

N: Total number of subjects.

The confidence intervals were calculated without multiplicity adjustment.

9.1.4.4 Wound Analysis

LIFE-BTK RCT collected comprehensive and quantitative wound data from a CLTI population. Wound care was not mandated or standardized in the trial. In the LIFE-BTK RCT, wounds present on the target limb were assessed by a wound core laboratory, using wound images taken by the investigator with a dedicated camera system provided by the core laboratory. Wounds were assessed at baseline to determine etiology and assessed for healing through 1 year. Wound images were required through 90-day follow-up. If the wound was not healed at 90 days, there was an additional assessment at 6- and 12-month follow-ups. Of the 184 wounds in 130 subjects (115 wounds in 85 subjects in the Esprit BTK arm and 69 wounds in 45 subjects in the PTA arm), 73.4% (71.3% in the Esprit BTK arm and 76.8% in the PTA arm) were assessed by the core laboratory as “arterial insufficiency only” wounds. The remaining wounds were assessed as “mixed etiology” wounds and included diabetic, venous stasis, traumatic, Charcot’s joint, and pressure-related wounds. The mean number of wounds per subject was 1.4 ±0.8 in the Esprit BTK arm and 1.5 ±0.9 in the PTA arm.

At 1 year, the cumulative percentage of index wounds healed was similar in both arms with 76.1% (54/71) of wounds healed in the Esprit BTK arm and 80% (40/50) in the PTA arm (Difference: -3.94%; 95% CI [-18.08%, 11.58%]), as shown in *Figure 9.1.4.4-1*. The cumulative percentage of subjects with healed index wound(s) was 44.6% (37/83) of wounds healed in the Esprit BTK arm and 55.6% (25/45) in the PTA arm (Difference: -10.98%; 95% CI [-27.91%, 6.94%]), as shown in *Figure 9.1.4.4-2*. Note that, for subjects presenting with more than one wound at index, all wounds had to be healed for a subject to be considered as having “wound healed”. It is important to note that the trial was not powered to detect differences in wound healing between the two arms.

Occurrence of new wounds, defined as wound below the knee in the index limb that was not identified at the time of the index procedure or wound that has recurred in the same location following the healing of the index wound, was a descriptive endpoint in LIFE-BTK RCT. The occurrence of new wound was 18.5% in the Esprit BTK arm and 14.8% in the PTA arm.

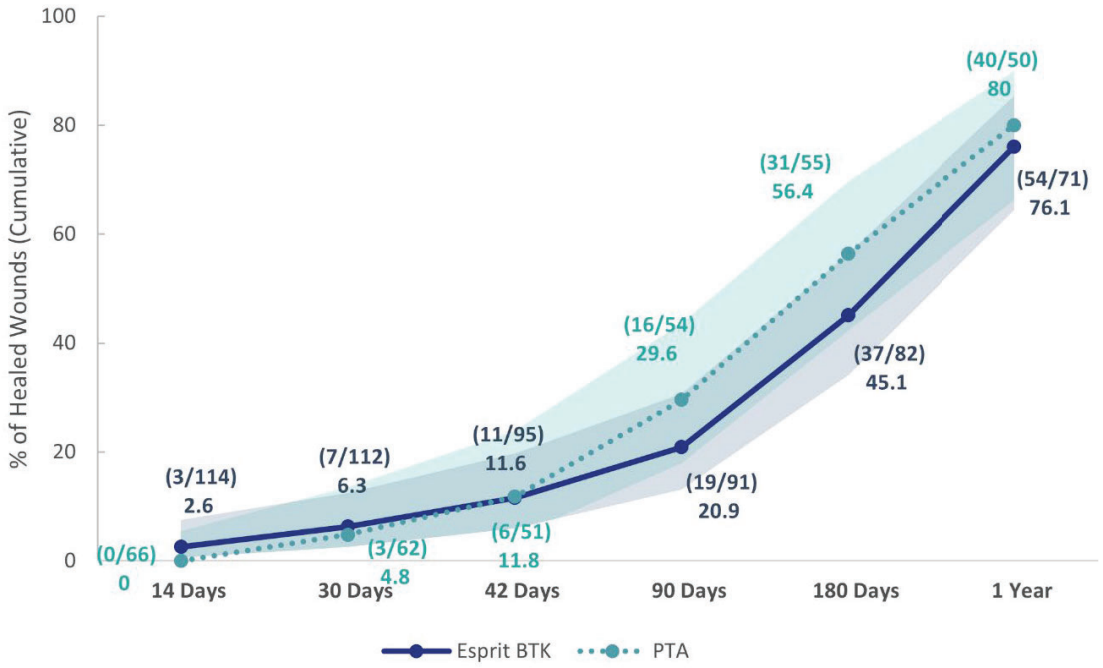


Figure 9.1.4.4-1: Cumulative Index Wound Healing at Each Timepoint – Wound-Level

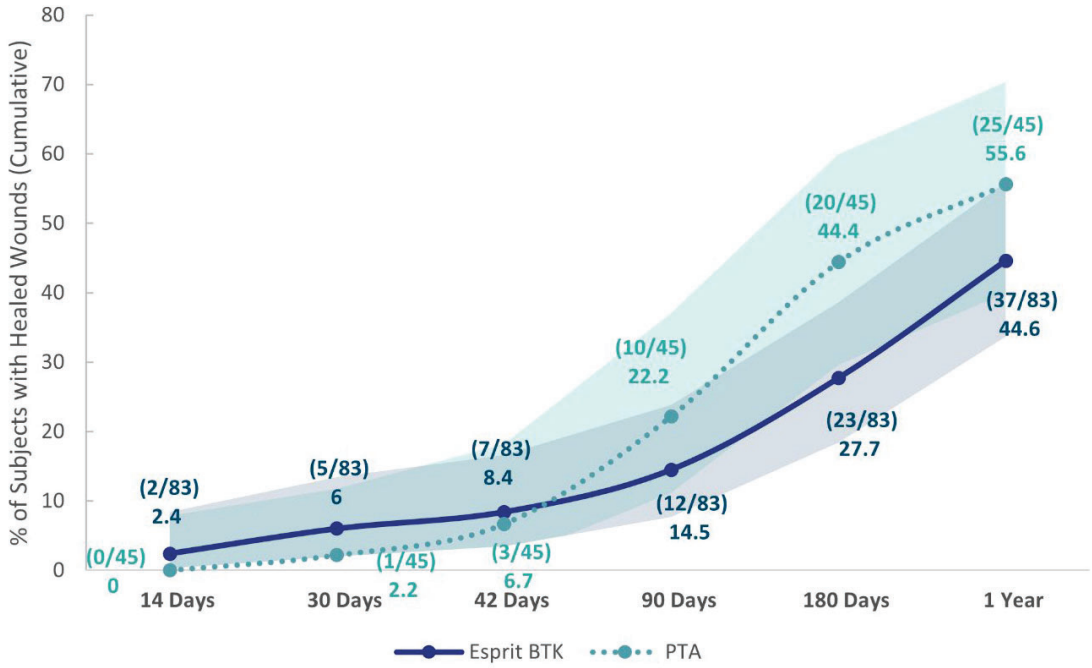


Figure 9.1.4.4-2: Cumulative Index Wound Healing at Each Timepoint – Subject-Level

9.1.4.5 Subgroup Analyses

The LIFE-BTK RCT results were analyzed by different pre-specified subgroups. Primary safety and effectiveness endpoints are shown for each subgroup in *Table 9.1.4.5.1-1, Table 9.1.4.5.2-1*, *Table 9.1.4.5.3-1*, *Table 9.1.4.5.4-1,* and *Table 9.1.4.5.4-2* below.

9.1.4.5.1 Gender Analysis

Female subjects represented 31.8% (83/261) of the randomized population. Compared to the overall population, females had similar event rates for the primary safety and primary effectiveness endpoints. The 5 events in the Esprit BTK arm for the primary safety endpoint all occurred in the male population, which represents 68.2% of the population enrolled in LIFE-BTK RCT. For the primary effectiveness endpoint, event rates in males and females were similar to the overall population. The observed difference in primary effectiveness endpoint rates between Esprit BTK and PTA arms, in both males and females, was consistent with the difference of about 30% in the overall population. The assessment of gender effect for the primary safety and effectiveness endpoints showed no significant treatment interaction by gender. Safety and effectiveness outcomes by gender subgroups are presented in *Table 9.1.4.5.1-1.*

Table 9.1.4.5.1-1: Primary Safety and Effectiveness Endpoints by Gender

	Esprit BTK	PTA	Interaction p-value
Primary Safety Endpoint – Freedom from MALE[1] at 6 months and POD at 30 days			
Male (N = 167) Female (N = 78)	95.4% (103/108) 100.0% (52/52)	100.0% (59/59) 100.0% (26/26)	0.9696
Primary Effectiveness Endpoint[2] – Limb Salvage and Primary Patency at 1 year			
Male (N = 148) Female (N = 72)	73.5% (72/98) 76.5% (39/51)	44.0% (22/50) 42.9% (9/21)	0.7546

Primary Safety Endpoint: As-Treated Population (N = 260) – Total evaluable population for primary safety endpoint: n = 245.

Primary Effectiveness Endpoint: Intent-to-Treat Population (N = 261) – Total evaluable population for primary effectiveness endpoint: n = 220.

Note: The treatment by subgroup interaction for the primary endpoints is evaluated using logistic regression, and the interaction p-value is provided. Interaction effect between treatment and gender on the primary endpoints is tested against an alpha level of 0.15.

N: Total number of subjects.
n: Number of evaluable subjects. For the primary safety endpoint, the following subjects were excluded from the evaluable population: subjects who terminated (due to withdrawal, lost-to-follow-up or post-30-day death) from the study prior to the lower limit (152 days) of the 6-month primary safety endpoint without any components of the primary safety endpoint. For the primary effectiveness endpoint, the following subjects were excluded from the evaluable population: subjects who terminated from the study (due to withdrawal, lost-to-follow-up or death) prior to the lower limit (337 days) of the 1-year primary effectiveness endpoint follow-up window without any components of the primary effectiveness endpoint. Subjects that did not have analyzable DUS or angiogram at 1-year and did not have primary effectiveness endpoint event prior to 1-year, were also excluded from the evaluable population.

[1] For the MALE component, the adverse event start date is used as the treatment date.

[2] For the amputation and CD-TLR components, the adverse event start date is used as the treatment date.

9.1.4.5.2 Race Analysis

The patient population enrolled in LIFE-BTK RCT was composed of 59% White and 12.3% Black or African American. The “other” subgroup included 18% Asian, 1.1% native Hawaiian or Other Pacific Islander, 0.4% American Indian or Alaska Native, and 4.3% of subjects who identified as “other” for their race. A total of 9.6% of subjects declined or were unable to disclose their race. Note that some subjects may have multiple races. Safety and effectiveness outcomes by race subgroups are presented in *Table 9.1.4.5.2-1.*

For the safety endpoint, all 5 events occurred in the White population, which represents the majority of the population enrolled in LIFE-BTK RCT.

For the endpoint of limb salvage and primary patency at 1 year, the lowest rate was observed in the White population, in the Esprit BTK arm, but still maintaining a 19.6% observed difference between Esprit BTK arm and PTA arm. In the other two race subgroups, event rates were similar to the overall population. The biggest difference between Esprit BTK and PTA arms (49.5%) was observed in the “Other” race subgroup, which was mainly composed of Asian subjects (94% in the primary safety endpoint analysis and 96% in the primary effectiveness endpoint analysis). Despite this observed difference, the assessment of race effect for the primary safety and effectiveness endpoints showed no significant treatment interaction by race.

Table 9.1.4.5.2-1: Primary Safety and Effectiveness Endpoints by Race (All Races) and Ethnicity

Primary Safety Endpoint – Freedom from MALE[1] at 6 months and POD at 30 days			
	Esprit BTK (N = 170)	**PTA (N = 90)**	**Interaction p-value**
Race			
White (N = 141)	94.4% (84/89)	100.0% (52/52)	0.9992
Black or African American (N = 30)	100.0% (19/19)	100.0% (11/11)	
Other (N = 50)	100.0% (35/35)	100.0% (15/15)	
Race (All Races)			
White (N = 141)	94.4% (84/89)	100.0% (52/52)	
Black or African American (N = 30)	100.0% (19/19)	100.0% (11/11)	
American Indian or Alaska Native (N = 1)	NA	100.0% (1/1)	NS
Asian (N = 47)	100.0% (35/35)	100.0% (12/12)	
Native Hawaiian or Other Pacific Islander (N = 3)	100.0% (1/1)	100.0% (2/2)	
Ethnicity			
Hispanic or Latino (N = 39)	89.3% (25/28)	100.0% (11/11)	NS
Not Hispanic or Latino (N = 193)	98.4% (122/124)	100.0% (69/69)	
Primary Effectiveness Endpoint[2] – Limb Salvage and Primary Patency at 1 year			
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Interaction p-value**
Race			
White (N = 123)	69.6% (55/79)	50.0% (22/44)	0.2041
Black or African American (N = 28)	77.8% (14/18)	40.0% (4/10)	
Other (N = 47)	82.9% (29/35)	33.3% (4/12)	
Race (All Races)			
White (N = 123)	69.6% (55/79)	50.0% (22/44)	
Black or African American (N = 28)	77.8% (14/18)	40.0% (4/10)	
American Indian or Alaska Native (N = 1)	NA	0.0% (0/1)	NS
Asian (N = 45)	82.9% (29/35)	40.0% (4/10)	
Native Hawaiian or Other Pacific Islander (N = 2)	100.0% (1/1)	0.0% (0/1)	
Ethnicity			
Hispanic or Latino (N = 37)	74.1% (20/27)	40.0% (4/10)	NS
Not Hispanic or Latino (N = 171)	74.6% (85/114)	43.9% (25/57)	

Primary Safety Endpoint: As-Treated Population (N = 260) – Total evaluable population for primary safety endpoint: n = 245.

Primary Effectiveness Endpoint: Intent-to-Treat Population (N = 261) – Total evaluable population for primary effectiveness endpoint: n = 220.

Note: The treatment by subgroup interaction for the primary endpoints is evaluated using logistic regression, and the interaction p-value is provided. Interaction effect between treatment and race on the primary endpoints is tested against an alpha level of 0.15.

NA: Not Available; NS: Not pre-specified; N: Total number of subjects.

n: Number of evaluable subjects. For the primary safety endpoint, the following subjects were excluded from the evaluable population: subjects who terminated (due to withdrawal, lost-to-follow-up or post-30-day death) from the study prior to the lower limit (152 days) of the 6-month primary safety endpoint without any components of the primary safety endpoint. For the primary effectiveness endpoint, the following subjects were excluded from the evaluable population: subjects who terminated from the study (due to withdrawal, lost-to-follow-up or death) prior to the lower limit (337 days) of the 1-year primary effectiveness endpoint follow-up window without any components of the primary effectiveness endpoint. Subjects that did not have analyzable DUS or angiogram at 1-year and did not have primary effectiveness endpoint event prior to 1-year, were also excluded from the evaluable population.

[1] For the MALE component, the adverse event start date is used as the treatment date.

[2] For the amputation and CD-TLR components, the adverse event start date is used as the treatment date.

9.1.4.5.3 Age Analysis

Of the 261 subjects randomized in the LIFE-BTK RCT, 76.2% (199/261 were ≥ 65 years old and 23.8% (62/261) were < 65 years old. Safety and effectiveness outcomes by age subgroups are presented in *Table 9.1.4.5.3-1*.

The primary safety endpoint rates in both age groups were consistent with the overall population. As for the primary effectiveness endpoint, observed rates for limb salvage and primary patency in the ≥ 65-year-old group were consistent with the overall population, with an observed difference of 33.1% between Esprit BTK and PTA arms. In the < 65-year-old group the observed difference between Esprit BTK and PTA arms was slightly lower (25.5%) but still favoring Esprit BTK arm. Despite these observed differences between age groups, the assessment of age effect for the primary safety and effectiveness endpoints showed no significant treatment interaction by age.

Table 9.1.4.5.3-1: Primary Safety and Effectiveness Endpoints by Age

Primary Safety Endpoint – Freedom from MALE[1] at 6-month and POD at 30 days			
	Esprit BTK (N = 170)	**PTA (N = 90)**	**Interaction p-value**
Age Age < 65 years (N = 58) Age ≥ 65 years (N = 187)	 94.3% (33/35) 97.6% (122/125)	 100.0% (23/23) 100.0% (62/62)	0.9983
Primary Effectiveness Endpoint[2] – Limb Salvage and Primary Patency at 1 year			
	Esprit BTK (N = 173)	**PTA (N = 88)**	**Interaction p-value**
Age Age < 65 years (N = 51) Age ≥ 65 years (N = 169)	 78.1% (25/32) 73.5% (86/117)	 52.6% (10/19) 40.4% (21/52)	0.7364

Primary Safety Endpoint: As-Treated Population (N = 260) – Total evaluable population for primary safety endpoint: n = 245.

Primary Effectiveness Endpoint: Intent-to-Treat Population (N = 261) – Total evaluable population for primary effectiveness endpoint: n = 220.

Note: The treatment by subgroup interaction for the primary endpoints is evaluated using logistic regression, and the interaction p-value is provided. Interaction effect between treatment and age on the primary endpoints is tested against an alpha level of 0.15.

N: Total number of subjects.

n: Number of evaluable subjects.

For the primary safety endpoint, the following subjects were excluded from the evaluable population: subjects who terminated (due to withdrawal, lost-to-follow-up or post-30-day death) from the study prior to the lower limit (152 days) of the 6-month primary safety endpoint without any components of the primary safety endpoint. For the primary effectiveness endpoint, the following subjects were excluded from the evaluable population: subjects who terminated from the study (due to withdrawal, lost-to-follow-up or death) prior to the lower limit (337 days) of the 1-year primary effectiveness endpoint follow-up window without any components of the primary effectiveness endpoint. Subjects that did not have analyzable DUS or angiogram at 1-year and did not have primary effectiveness endpoint event prior to 1-year, were also excluded from the evaluable population.

[1] For the MALE component, the adverse event start date is used as the treatment date.

[2] For the amputation and CD-TLR components, the adverse event start date is used as the treatment date.

9.1.4.5.4 Analysis by Lesion Length Terciles

To assess the performance of the Esprit BTK System, as compared to PTA, across the continuum of lesion lengths treated in the LIFE-BTK RCT, a post-hoc subgroup analysis by lesion length terciles was conducted and is presented in *Tables 9.1.4.5.4-1* and *9.1.4.5.4-2*.

Target lesion lengths in LIFE-BTK RCT ranged from 3.82 mm to 148.40 mm, by core laboratory assessment. Target lesion lengths ranged from 3.82 mm to 24.74 mm in the first tercile (short), from 24.75 mm to 52.82 mm in the second tercile (medium), and from 53.00 mm to 148.40 mm in the third tercile (long). The mean number of scaffolds implanted ranged from 1.1 ±0.4 scaffolds in the first tercile to 3.3 ±1.4 in the third tercile. In all 3 lesion length tercile subgroups, the primary effectiveness endpoint results were consistent with the overall population, with an observed difference between Esprit BTK and PTA arms ranging from 27.55% to 30.36%.

Table 9.1.4.5.4-1: Target Lesion Length Terciles by Treatment Arm

	First Tercile (Short)		Second Tercile (Medium)		Third Tercile (Long)	
	Esprit BTK (N = 61)	**PTA (N = 24)**	**Esprit BTK (N = 53)**	**PTA (N = 32)**	**Esprit BTK (N = 54)**	**PTA (N = 31)**
Target Lesion Length per Subject						
Mean ±SD	15.34 ±5.64	15.95 ±5.18	36.79 ±8.51	35.60 ±7.09	82.41 ±24.90	78.45 ±20.36
Range (min, max)	(3.82, 24.71)	(5.33, 24.74)	(24.99, 52.82)	(24.75, 51.97)	(53.00, 148.40)	(53.22, 125.10)
Number of Scaffolds Used per Subject						
Mean ±SD	1.1 ±0.4	NA	1.6 ±0.9	NA	3.3 ±1.4	NA
Range (min, max)	(1, 3)		(1, 5)		(1, 6)	

Note: The longest lesion length is used per subject.

N: Total number of subjects. NA: Not applicable.

Table 9.1.4.5.4-2: Primary Effectiveness Endpoint by Lesion Length Terciles

	Total Number of Subjects Analyzed	**Esprit BTK (N = 173)**	**PTA (N = 88)**	**Difference [95% CI][1]**
Lesion Length Tercile	215			
First Tercile (Short)	72	83.3% (45/54)	55.6% (10/18)	27.78% [4.52%, 50.92%]
Second Tercile (Medium)	77	77.6% (38/49)	50.0% (14/28)	27.55% [5.60%, 47.31%]
Third Tercile (Long)	66	59.5% (25/42)	29.2% (7/24)	30.36% [5.34%, 49.94%]

[1] By Newcombe score method.

N: Total number of subjects.
The confidence intervals were calculated without any multiplicity adjustment.

9.1.4.6 Site-Reported Serious Adverse Events

Table 9.1.4.6-1 provides a summary of the site-reported serious adverse events (SAE) observed in the LIFE-BTK RCT through 1 year. SAE in this study is defined as an event that:

- Led to a death,
- Led to a serious deterioration in health of the subject, that either resulted in:
  - a life-threatening illness or injury, or
  - a permanent impairment of a body structure or a body function, or
  - in-patient hospitalization or prolongation of existing hospitalization, or
  - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
  - chronic disease
- Led to fetal distress, fetal death or a congenital abnormality or birth defect.

In *Table 9.1.4.6-1*, the incidence rate and number of serious adverse events were tabulated by MedDRA system organ class (SOC). The percentages of subjects with SAEs, as reported by the investigators, were similar in both arms (51.4% in the Esprit BTK arm and 51.1% in the PTA arm). The most reported events per system organ class were injury, poisoning, and procedural complications, and infections and infestations, in both arms.

Table 9.1.4.6-1: Summary of Site-Reported Serious Adverse Events through 1 Year – Intent-to-Treat (N = 261)

System Organ Class Preferred Term	Total		Esprit BTK		PTA	
	Number of Events	Number of Subjects (N = 261)	Number of Events	Number of Subjects (N = 173)	Number of Events	Number of Subjects (N = 88)
Any SAE	349	51.3% (134/261)	252	51.4% (89/173)	97	51.1% (45/88)
Blood And Lymphatic System Disorders	7	2.3% (6/261)	3	1.7% (3/173)	4	3.4% (3/88)
Cardiac Disorders	36	7.3% (19/261)	30	8.1% (14/173)	6	5.7% (5/88)
Gastrointestinal Disorders	8	2.7% (7/261)	8	4.0% (7/173)	0	0.0% (0/88)
General Disorders and Administration Site Conditions	16	5.0% (13/261)	12	5.2% (9/173)	4	4.5% (4/88)
Hepatobiliary Disorders	2	0.4% (1/261)	2	0.6% (1/173)	0	0.0% (0/88)
Infections And Infestations	47	12.6% (33/261)	32	13.9% (24/173)	15	10.2% (9/88)
Injury, Poisoning, And Procedural Complications	74	21.1% (55/261)	55	22.5% (39/173)	19	18.2% (16/88)
Investigations	4	1.5% (4/261)	1	0.6% (1/173)	3	3.4% (3/88)
Metabolism And Nutrition Disorders	5	1.9% (5/261)	4	2.3% (4/173)	1	1.1% (1/88)
Musculoskeletal And Connective Tissue Disorders	21	6.5% (17/261)	15	6.9% (12/173)	6	5.7% (5/88)
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	3	1.1% (3/261)	0	0.0% (0/173)	3	3.4% (3/88)
Nervous System Disorders	17	5.4% (14/261)	11	5.8% (10/173)	6	4.5% (4/88)
Psychiatric Disorders	2	0.8% (2/261)	0	0.0% (0/173)	2	2.3% (2/88)
Renal And Urinary Disorders	18	5.7% (15/261)	12	5.8% (10/173)	6	5.7% (5/88)
Respiratory, Thoracic and Mediastinal Disorders	21	6.9% (18/261)	17	8.1% (14/173)	4	4.5% (4/88)
Skin And Subcutaneous Tissue Disorders	9	3.1% (8/261)	8	4.0% (7/173)	1	1.1% (1/88)
Surgical And Medical Procedures	22	8.0% (21/261)	16	8.7% (15/173)	6	6.8% (6/88)
Vascular Disorders	37	10.7% (28/261)	26	11.6% (20/173)	11	9.1% (8/88)

Note: Include adverse events only on or post index procedures.
The numerator counts only each subject's first occurrence of each event.
N: Total number of subjects.

9.1.5 Conclusion

The LIFE-BTK RCT met both co-primary endpoints. The primary safety endpoint (freedom from Major Adverse Limb Event (MALE) at 6 months + Peri-Operative Death (POD) at 30 days) assessment showed non-inferiority of the Esprit BTK arm compared to the PTA arm, with a p-value of 0.0019. The primary effectiveness endpoint assessment showed superiority of the Esprit BTK arm over the PTA arm at 1 year, with a p-value of < 0.0001.

Both powered secondary endpoints were also met. The Esprit BTK arm showed superiority to the PTA arm in target lesion binary restenosis rate at 1-year, with a p-value of < 0.0001, and in the composite endpoint of freedom from above ankle amputation in the index limb, 100% total occlusion of the target vessel, and CD-TLR rate at 1 year, with a p-value of 0.0081.

In conclusion, the LIFE-BTK RCT results support the safety and effectiveness of the Esprit BTK System for the planned treatment of diseased infrapopliteal lesions in patients with chronic limb-threatening ischemia (CLTI).

10.0 INDIVIDUALIZATION OF TREATMENT

The risk and benefits should be considered for each patient before using the Esprit™ BTK System. Patient selection factors to be assessed should include assessment of inflow and outflow vessels (and whether these vessels require treatment), identifying appropriately sized below-the-knee vessels for Esprit™ BTK Scaffold implantation, and judgement regarding the potential for non-compliance with antiplatelet therapy.

In LIFE-BTK trial, significant lesions (≥ 50% stenosis) in inflow arteries had to be treated successfully prior to subject registration into the trial.

Quantitative imaging is strongly recommended to accurately measure and confirm appropriate vessel sizing (reference vessel diameter ≥ 2.5 mm). If quantitative imaging determines a vessel size < 2.5 mm, do not implant the Esprit BTK Scaffold.

Antiplatelet drugs should be used in combination with the Esprit BTK System. It is strongly advised that the treating physicians consult the Trans-Atlantic Inter-Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy to reduce the risk of scaffold thrombosis. Physicians should use the information from the LIFE-BTK trial, coupled with current literature on drug-eluting stents / scaffolds for lower limb and the specific needs of individual patients, to determine the specific antiplatelet drug dose and duration to be used for the patients in general practice. In the LIFE-BTK trial, all subjects receiving Esprit™ BTK Scaffolds were maintained on dual antiplatelet therapy [aspirin and a P2Y12 receptor inhibitor (clopidogrel, prasugrel or ticagrelor)] for a minimum of 12 months post-procedure.

Patients who require premature discontinuation of antiplatelet therapy secondary to significant active bleeding, or the expectation of significant bleeding, should be monitored carefully for lower limb events, and once stabilized, have their antiplatelet therapy restarted as soon as possible per the discretion of treating physicians.

11.0 PATIENT COUNSELING AND PATIENT INFORMATION

Physicians should consider the following in counseling patients in connection with this device:

- Discuss the risks associated with the scaffold placement and the benefits for this particular patient.
- Discuss the importance of taking prescribed medications (such as antiplatelet therapy) after scaffold procedure.
- Discuss the risks of allergic reaction or hypersensitivity to device components.
- Discuss lifestyle changes following the procedure and over the long term.

  For patients presenting with wound on the lower limb, discuss the importance of appropriate wound care.

The following patient materials are provided for this product:

- A patient information guide, including information on PAD, the implant procedure and the Esprit™ BTK System (provided online at: vascular.eIFU.abbott).
- A device implant card, including both patient information and scaffold implant information (provided in package).

12.0 CLINICIAN USE INFORMATION

12.1 Vessel Sizing and Scaffold Size Selection

- **Quantitative imaging is recommended** for the assessment of reference vessel diameter at baseline for appropriate Esprit™ BTK Scaffold size selection.

- Quantitative imaging is strongly recommended to accurately measure and confirm appropriate vessel sizing reference vessel diameter ≥ 2.5 mm). If quantitative imaging determines a vessel size < 2.5 mm, do not implant the Esprit BTK Scaffold. (see *Section 5.0 Warnings*)

- The reference vessel diameter ranges to be treated in the procedure are indicated in *Table 12.1-1*, along with the Esprit BTK Scaffold diameter to be used in order to achieve 1:1 sizing of the vessel to the scaffold.

Table 12.1-1: Reference Vessel Diameter Ranges and Esprit BTK Scaffold Diameter to be Used (Quantitative Imaging)

Reference Vessel Diameter	Esprit BTK Scaffold Diameter to be Used
≥ 2.50 mm and ≤ 2.75 mm	2.50 mm
≥ 2.50 mm and ≤ 3.00 mm	2.75 mm
≥ 2.75 mm and ≤ 3.25 mm	3.00 mm
≥ 3.25 mm and ≤ 3.75 mm	3.50 mm
≥ 3.50 mm and ≤ 4.00 mm	3.75 mm

- Size the scaffold to the proximal reference vessel diameter of the scaffold's landing zone.

  Note: Refer to *Table 12.7-1* for appropriate scaffold diameters.

- **If visual estimation is used:**

  - **Use the pre-dilatation balloon, when inflated, to assist in sizing the vessel.**
  - **Consider upsizing the scaffold for in-between diameters to ensure appropriate expansion.**

  For cases where the combination of reference vessel diameter and target lesion length are appropriate to be treated by more than one scaffold size, the selection of scaffold size can be made per the judgment of the physician.

  Note: The labeled scaffold diameter refers to the nominal expanded scaffold inner diameter.

12.2 Inspection Prior to Use

- Carefully inspect the sterile package before opening and check for damage. Do not use if the integrity of the sterile package has been compromised.
- Do not use after the “Use by” date.
- Open the pouch and pass or drop the product into the sterile field using an aseptic technique.
- Prior to using the Esprit™ BTK System, carefully remove the system from the package and inspect for bends, kinks, and other damage. Verify that the scaffold does not extend beyond the radiopaque balloon markers. Do not use if any device defects are noted. **Do not manipulate, touch, or handle the scaffold**, which may cause coating damage, contamination, or scaffold dislodgement from the delivery balloon.

  Note: At any time during the use of the Esprit BTK System, if the hypotube has been bent or kinked, do not continue to use the catheter.

12.3 Materials Recommended

- 5F / 0.070" / 1.8 mm minimum inner diameter introducer sheath of appropriate shape for the target vessel
- 2 – 3 syringes (10 – 20 cc)
- 1,000 u/500 cc heparinized normal saline (HepNS)
- Rotating hemostatic valve with appropriate minimum inner diameter (0.096” [2.44 mm])
- 0.014" (0.36 mm) x 175 cm (minimum length) guide wire
- Torque device
- Guide wire introducer
- Contrast diluted 1:1 with heparinized normal saline
- Appropriate-size pre-dilatation angioplasty balloon
- Appropriate-size post-dilatation non-compliant angioplasty balloon
- Inflation device
- Three-way stopcock
- Appropriate anticoagulation and antiplatelet drugs

12.4 Preparation

12.4.1 Packaging Removal

Note: The foil pouch is the sterile barrier. Sterile product is contained within this one pouch — there is no secondary pouch.

- Peel the pouch open from the top corner.
- Carefully remove the scaffold system from its protective tubing for preparation of the device.
- Do not bend or kink the hypotube during removal.

12.4.2 Dual Layer Sheath Removal

1. While holding the distal catheter shaft with one hand, grasp only the yellow outer sheath with the other hand and gently slide the sheath distally.
2. A longitudinal split on the inner sheath will open up and be visible.
3. The stylet and dual layer sheath are removed simultaneously from the delivery system by continuing to slide the yellow sheath distally until the inner and outer layers of the dual layer sheath as well as the stylet are free from the catheter.
   see *Section 6.3 Scaffold Handling*. Do not use the device if the sheath cannot be removed as indicated.
4. Verify that the scaffold does not extend beyond the radiopaque balloon markers and no scaffold struts are lifted. **Do not use if any device defects are noted.**
5. If unusual resistance is felt during product stylet and scaffold sheath removal, do not use this product, and instead replace with another.

12.4.3 Guide Wire Lumen Flush

Use a sterile, HepNS filled syringe, and place the distal tip of the delivery system slightly within the tip of the syringe. Flush the guide wire lumen with HepNS until fluid exits the guide wire exit notch (RX notch).

Note: Do not place the scaffold within the syringe. Avoid manipulation of the scaffold while flushing the guide wire lumen as this may disrupt the placement of the scaffold on the balloon.

12.4.4 Delivery System Preparation

1. Prepare an inflation device / syringe with diluted contrast medium.
2. Attach an inflation device / syringe to the stopcock; attach it to the inflation port of the product. Do not bend the product hypotube when connecting to the inflation device / syringe.
3. With the tip down, orient the delivery system vertically.
4. Open the stopcock to the delivery system; pull negative for approximately 30 seconds; release to neutral for contrast fill.
5. Close the stopcock to the delivery system; purge the inflation device / syringe of all air.
6. Repeat steps 3 through 5 until all air is expelled. If bubbles persist, do not use the product.
7. If a syringe was used, attach a prepared inflation device to the stopcock.
8. Open the stopcock to the delivery system.
9. Leave on neutral.

Note: While introducing the scaffold system into the vessel, do not induce negative pressure on the delivery system. This may cause dislodgement of the scaffold from the balloon.

Note: If air is seen in the shaft, repeat *Section 12.4.4 Delivery System Preparation,* steps 3 through 5, to prevent uneven scaffold expansion.

12.5 Delivery Procedure

1. Prepare the vascular access site according to standard practice.
2. Adequate lesion preparation prior to scaffold implantation is required to ensure safe delivery of the scaffold across the target lesion.
3. **Pre-dilate the lesion to match the reference vessel diameter with a percutaneous transluminal angioplasty catheter.** Pre-dilatation should be performed with an angioplasty balloon which can also be utilized to properly size the vessel.

   Note: Limit the length of the pre-dilatation by the PTA balloon to avoid creating a region of vessel injury that is outside the boundaries of the Esprit BTK Scaffold.
4. Maintain neutral pressure on the inflation device.
5. Open the rotating hemostatic valve as wide as possible (if used).
6. Backload the delivery system onto the proximal portion of the guide wire, while maintaining guide wire position across the target lesion.
7. Carefully advance the delivery system into the introducer sheath and over the guide wire to the target lesion. When using a rapid exchange (RX) system, be sure to keep the hypotube straight.

   Note: If unusual resistance is felt before the scaffold exits the introducer catheter, do not force passage. Resistance may indicate a problem and the use of excessive force may result in scaffold damage or dislodgement. Maintain guide wire placement across the lesion and remove the delivery system and introducer sheath as a single unit.
8. Advance the delivery system over the guide wire to the target lesion under direct fluoroscopic visualization. Utilize radiopaque balloon markers to position the scaffold across the lesion; perform angiography to confirm scaffold position. If the position of the scaffold is not optimal, it should be carefully repositioned or removed (see *Section 6.6 Scaffold / System Removal*). The balloon markers indicate both the scaffold edges and the balloon shoulders. Expansion of the scaffold should not be undertaken if the scaffold is not properly positioned in the target lesion.

   Note: If removal of a scaffold system is required prior to deployment, ensure that the introducer sheath is coaxially positioned relative to the scaffold delivery system and cautiously withdraw the scaffold system into the introducer sheath. **Should unusual resistance** be felt at **any time** when withdrawing the scaffold into the introducer sheath, the scaffold delivery system and the introducer or introducer sheath should be **removed as a single unit**. This should be done under direct visualization with fluoroscopy. This scaffold cannot be reinserted.
9. If utilizing multiple scaffolds, overlap the balloon marker band of the undeployed scaffold with the markers of the most recently deployed scaffold, prior to expansion. When possible, minimize scaffold overlap or gap.

   Note: When deploying multiple scaffolds within the same vessel, it is recommended to deploy distally to proximally to minimize passing devices through recently deployed scaffolds.
10. Tighten the rotating hemostatic valve (if used)
11. The scaffold is now ready to be deployed.

12.6 Deployment Procedure

CAUTION: Refer to product label for *in vitro* scaffold inner diameter, nominal pressure, and rated burst pressure (RBP).

1. Prior to deployment, reconfirm the correct position of the scaffold relative to the target lesion using the radiopaque balloon markers.
2. Using fluoroscopic visualization, deploy the scaffold slowly, by pressurizing the delivery system in **2-atm increments over 5 seconds**, until the scaffold is completely expanded. Maintain final pressure for 30 seconds. Fully expand the scaffold by inflating to nominal pressure, at a minimum. Accepted practice generally targets an initial deployment pressure that would achieve a scaffold inner ratio of about 1.1 times the reference vessel diameter. Optimal scaffold expansion and proper apposition require that the scaffold be in full contact with the arterial wall.

   CAUTION: Do not exceed the labeled RBP of 16 atm (1621 kPa) or maximum deployment diameter of the scaffold (See *Section 14.0 IN VITRO COMPLIANCE INFORMATION* and *Table 12.7-1*).
3. Expand scaffold to nominal pressure at minimum. Maintain final pressure for 30 seconds. If necessary, the delivery system can be repressurized or further pressurized to ensure complete apposition of the scaffold to the artery wall.

   Fully cover the entire lesion and balloon-treated area (including dissections) with the Esprit BTK Scaffold, allowing for adequate scaffold coverage into healthy tissue proximal and distal to the lesion.
4. Deflate the balloon by pulling negative on the inflation device for 30 seconds. Confirm complete balloon deflation before attempting to move the delivery system. If unusual resistance is felt during scaffold delivery system withdrawal, pay particular attention to the introducer sheath position.

   Note: See *Section 12.8 Removal Procedure* for instruction on withdrawal of scaffold delivery system.
5. Confirm scaffold position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the scaffold. Fluoroscopic visualization during scaffold expansion should be used in order to properly judge the optimum expanded scaffold diameter as compared to the proximal and distal artery diameter(s). **Optimal expansion requires that the scaffold be in full contact with the artery wall**. Scaffold to vessel wall contact may be verified through intravascular imaging.
6. **Post-dilatation with a non-compliant angioplasty balloon is strongly recommended for optimal scaffold apposition.** When performed, follow the instructions in *Section 12.7 Further Expansion of the Deployed Scaffold*, as long as the post-dilatated segment is within the allowable expansion limits of the scaffold.

12.7 Further Expansion of the Deployed Scaffold

1. **DEPLOYED SCAFFOLDS SHOULD NOT BE LEFT UNDER-DILATED.**

   Deployed scaffolds should be well-apposed to the vessel wall. To achieve optimal scaffold apposition, post-dilatation with a non-compliant angioplasty balloon is strongly recommended, especially for small vessels. When performed with a non-compliant balloon, post-dilatation should be at high pressure (> 16 atm)*.

   ***Note**: Limit choice of non-compliant balloon nominal diameter to be no more than 0.5 mm above the scaffold nominal diameter to stay within the scaffold's maximum expansion limit. **The compliance chart of the non-compliant balloon selected must be carefully reviewed prior to dilatation and an appropriate maximum pressure used to ensure that the scaffold is not over dilated.**

   The scaffold segment should be carefully crossed to avoid disrupting the scaffold geometry. Use of a prolapsed guide wire can be one recommended approach. Post-dilatation must only be done with balloons sized to fit within the boundaries of the scaffold.

   CAUTION: Do not exceed the scaffold labeled rated burst pressure (RBP) of 16 atm (1621 kPa).

   CAUTION: Do not dilate the scaffold beyond the maximum post-dilatation diameter which is 0.5 mm above the nominal diameter (see *Table 12.7-1*). Over-dilatation may result in scaffold damage.

Table 12.7-1: Nominal Scaffold Diameter and Dilatation Limit

Nominal Scaffold Diameter	Dilatation Limit
2.50 mm	3.00 mm Maximum post-dilatation diameter
2.75 mm	3.25 mm Maximum post-dilatation diameter
3.00 mm	3.50 mm Maximum post-dilatation diameter
3.50 mm	4.00 mm Maximum post-dilatation diameter
3.75 mm	4.25 mm Maximum post-dilatation diameter

2. **Ensure** the final scaffold diameter matches the reference vessel diameter to **ENSURE GOOD SCAFFOLD APPOSITION**. Reconfirm scaffold position and angiographic results. Repeat inflations until achieved.

12.8 Removal Procedure

Withdrawal of the scaffold delivery system / post-dilatation balloon from the deployed scaffold:

1. Deflate the balloon by pulling negative on the inflation device. Larger and longer balloons will take more time (up to 30 seconds) to deflate than smaller and shorter balloons. Confirm balloon deflation under fluoroscopy and wait 10 – 15 seconds longer.
2. Position the inflation device to "negative" or "neutral" pressure.

3. Stabilize the introducer sheath position just outside the ostium and anchor in place.
4. Maintain guide wire placement across scaffolded segment.
5. Open the rotating hemostatic valve (if used).
6. Gently remove the scaffold delivery system with slow and steady pressure.
7. Tighten the rotating hemostatic valve (if used).

If during withdrawal of the catheter from the deployed scaffold, resistance is encountered, use the following steps to improve balloon rewrap:

- Re-inflate the balloon up to nominal pressure, deflate and change pressure to neutral.
- Repeat steps 1 – 7 above.
- Re-evaluate the scaffolded region once the balloon is removed to ensure optimal apposition.

Note: See *Section 6.6 Scaffold / System Removal* for specific delivery system removal instructions.

Post-scaffold delivery system withdrawal – scaffold deployment confirmation

1. Confirm scaffold position and deployment using standard angiographic techniques. For optimal results, the entire stenosed arterial segment should be covered by the scaffold. Fluoroscopic visualization during scaffold expansion should be used in order to properly judge the optimum expanded scaffold diameter as compared to the proximal and distal artery diameter(s). **Optimal expansion requires that the scaffold be in full contact with the artery wall**. Scaffold to vessel wall contact may be verified through intravascular imaging.
2. Reconfirm scaffold position and angiographic results to assess scaffolded area. Repeat inflations until optimal scaffold deployment is achieved. If post-dilatation is necessary, ensure that the final scaffold diameter matches the reference vessel diameter. Intravascular imaging can be utilized to **ensure the scaffold struts are in contact with the inner luminal wall of the artery and that the scaffold has been optimally expanded.**

13.0 DISPOSAL INSTRUCTIONS

After use, this device, its accessories, and packaging should be appropriately classified for disposal (e.g., battery, biohazard, sharp, non-hazardous waste, etc.) and carefully disposed of in compliance with facility procedures and applicable laws and regulations.

14.0 *IN VITRO* COMPLIANCE INFORMATION

Table 14.0-1: Esprit™ BTK Scaffold Compliance

System Diameter (mm)	Scaffold Inner Diameter (ID) by Pressure												
	6 atm	7 atm	8 atm	9 atm (NOM)	10 atm	11 atm	12 atm	13 atm	14 atm	15 atm	16 atm (RBP)*	17 atm	18 atm
	608 kPa	**709 kPa**	**811 kPa**	**912 kPa**	**1013 kPa**	**1115 kPa**	**1216 kPa**	**1317 kPa**	**1419 kPa**	**1520 kPa**	**1621 kPa**	**1723 kPa**	**1824 kPa**
2.5	2.36 mm	2.41 mm	2.45 mm	**2.48 mm**	2.51 mm	2.54 mm	2.56 mm	2.59 mm	2.61 mm	2.63 mm	**2.65 mm**	2.68 mm	2.70 mm
2.75	2.58 mm	2.64 mm	2.69 mm	**2.73 mm**	2.76 mm	2.80 mm	2.82 mm	2.85 mm	2.88 mm	2.90 mm	**2.93 mm**	2.95 mm	2.98 mm
3.0	2.84 mm	2.91 mm	2.97 mm	**3.01 mm**	3.06 mm	3.09 mm	3.12 mm	3.15 mm	3.17 mm	3.20 mm	**3.22 mm**	3.25 mm	3.27 mm
3.5	3.24 mm	3.31 mm	3.38 mm	**3.43 mm**	3.48 mm	3.52 mm	3.56 mm	3.59 mm	3.63 mm	3.66 mm	**3.69 mm**	3.71 mm	3.75 mm
3.75	3.53 mm	3.62 mm	3.69 mm	**3.75 mm**	3.80 mm	3.84 mm	3.88 mm	3.91 mm	3.94 mm	3.98 mm	**4.01 mm**	4.04 mm	4.08 mm

Note: These nominal data are based on *in vitro* testing at 37°C and do not take into account lesion resistance. Ensure full deployment of the scaffold (see *Section 12.6 Deployment Procedure*) and confirm the scaffold sizing angiographically.
*Do not exceed the rated burst pressure (RBP).

Abbott Medical
3200 Lakeside Drive
Santa Clara, CA 95054 USA

CUSTOMER SERVICE
TEL: (800) 227-9902
FAX: (800) 601-8874
Outside USA TEL: +1 951-914-4669
Outside USA FAX: +1 951-914-2531

Graphical Symbols for Medical Device Labeling

Manufacturer	Consult instructions for use or consult electronic instructions for use	MD Medical device	Packaging unit
RX Rapid exchange	Caution	REF Catalogue number	Open here
MR MR Conditional	Do not re-use	Date of manufacture	Single sterile barrier system
Do not use if package is damaged and consult instructions for use	STERILIZE Do not resterilize	LOT Batch code	Non-pyrogenic
Keep dry	Keep away from sunlight	F French size	Inner diameter
Use-by date	REC MIN SHEATH Recommended minimum sheath	Contains a medicinal substance	UDI Unique device identifier
STERILE R Sterilized using irradiation	Upper limit of temperature	EXCURSIONS Excursions permitted to temperature	Separate collection for waste electrical / electronic equipment
POST DILATATION LIMIT Post dilatation limit	Balloon-Expandable PLLA Scaffold Balloon-Expandable PLLA Scaffold	℞ ONLY CAUTION: Federal law restricts this device to sale by or on the order of a physician	