Boston Scientific

ELUVIA™

OVER-THE-WIRE

Drug-Eluting Vascular Stent System

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BSC (MB eIFU Template 8.2677 x 11.6929 A4, 92524324F), eIFU, MB, Eluvia, en, 51574536-01A

℞ **ONLY**

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

1. WARNING

A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2 years - 3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. See Section 8.1 for further information.

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For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization 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 may lead to injury, illness or death of the patient.

After use, dispose of product and packaging in accordance with hospital, administrative and/or local government policy.

Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions. Failure to do so may result in complications.

STERILE – DO NOT RESTERILIZE – SINGLE USE ONLY

2. DEVICE DESCRIPTION

The ELUVIA Drug-Eluting Vascular Stent System is a device/drug combination product composed of: a device (stent system) and a drug coating (a formulation of paclitaxel contained in a polymer matrix). The characteristics of the ELUVIA Stent System are described in **Table 2-1.**

Table 2-1. ELUVIA Drug-Eluting Vascular Stent System Product Description

ELUVIA Drug-Eluting Vascular Stent System	
Available Stent Lengths (mm)	40, 60, 80, 100, 120, 150
Available Stent Diameters (mm)	6, 7
Stent Material	Nickel Titanium Alloy (NiTi)

ELUVIA Drug-Eluting Vascular Stent System	
Drug Product	A conformal coating of a polymer carrier consisting of paclitaxel (10 % by weight) and PVDF (polyvinylidene difluoride 90 % by weight) with a maximum nominal drug content of 517 µg on the largest stent (7.0 mm x 150 mm).
Average Stent Length Change At Vessel Diameter	The ELUVIA deployed stent length change from the delivery system is approximately 3 % on average or less.
Delivery System Effective Length	75 cm, 130 cm

User Information

Only physicians who are familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with superficial femoral and/or proximal popliteal artery interventional procedures should use this device.

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Quantity	Material
One (1)	ELUVIA Stent with Delivery System

2.1 Device Component Description

The stent system is comprised of the implantable endoprosthesis and the stent delivery system. The stent is a laser cut self-expanding stent composed of a nickel titanium alloy (nitinol). On both the proximal and distal ends of the stent, radiopaque markers made of tantalum increase visibility of the stent to aid in placement. The stent is constrained within a 6F (2.1 mm maximum OD) delivery system. The delivery system is a triaxial design with an outer shaft to stabilize the stent delivery system, a middle shaft to protect and constrain the stent, and an inner shaft to provide a guidewire lumen. Shaft components contain a proprietary silicone based lubricious coating that extends the entire length of each component, which is intended to reduce deployment forces. The coating is not on the outer surface of the device, therefore there is no exposure of the coating to ancillary devices or to the vasculature during device preparation and tracking to the deployment site. The delivery system is compatible with 0.035 in (0.89 mm) guidewires.

The ELUVIA Drug-Eluting Vascular Stent is available in a variety of diameters and lengths. The delivery system is also offered in two working lengths (75 cm and 130 cm).

2.2 Drug Component Description

The ELUVIA Drug-Eluting Vascular Stent is a stent with a drug/polymer coating. The coating is comprised of two layers: the inner layer consists of a polymer (PBMA) which is a primer for improving the adhesion of the outer layer; the outer layer is a drug/polymer coating formulation consisting of paclitaxel (the active ingredient), and PVDF-HFP Polymer Carrier (the inactive ingredient).

2.2.1 Paclitaxel Drug

The active pharmaceutical ingredient is semi-synthetic paclitaxel. Semi-synthetic paclitaxel is synthesized from precursor compounds isolated from a spectrum of Taxus species and hybrids. The chemical name of paclitaxel is: Benzenepropanoic acid, β-(benzoylamino)-α-hydroxy-,6, 12b-bis(acetyloxy)-12-(benzoyloxy)-2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b-dodecahydro-4, 11-dihydroxy-4a, 8, 13, 13-tetramethyl-5-oxo-7, 11-methano-1H-cyclodeca [3, 4]benz [1, 2-b]-oxet-9-ylester, [2aR-[2aα, 4β, 4aβ, 6β, 9α(αR, βS), 11α, 12α, 12aα, 12bα]].

Paclitaxel is a diterpenoid with a characteristic taxane skeleton of 20 carbon atoms, a molecular weight of 853.91 g/mol and a molecular formula of $C_{47}H_{51}NO_{14}$. It is highly lipophilic, insoluble in water, but freely soluble in methanol, ethanol, chloroform, ethyl acetate and dimethyl sulfoxide.

The chemical structure of paclitaxel is shown in **Figure 1**.

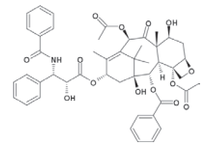

Figure 1. Chemical Structure of Paclitaxel (PTx)

2.2.2 Primer Polymer and Drug Matrix Copolymer Carrier

The stent contains a primer polymer layer PBMA - poly(n-butyl methacrylate) between the bare metal stent and drug matrix layer. The chemical structure of PBMA is provided below in **Figure 2**.

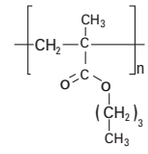

Figure 2. PBMA - poly(n-butyl methacrylate)

The drug matrix layer is comprised of a semi-crystalline random copolymer, PVDF-HFP - poly(vinylidene fluoride-co-hexafluoropropylene), blended with paclitaxel. The chemical structure of PVDF-HFP is provided below in **Figure 3**.

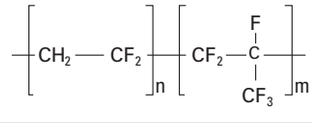

Figure 3. PVDF-HFP- poly(vinylidene fluoride-co-hexafluoropropylene)

2.3 Product Matrix and Paclitaxel Content

Table 2-2. ELUVIA Drug-Eluting Vascular Stent System Product Matrix and Paclitaxel Content

	Stent Nominal Diameter (mm)	Unconstrained Length (mm)	Stent Length at Vessel Diameter (mm)	Foreshortening (%)	Working Length (cm)	Reference Vessel Diameter (mm)	Nominal Paclitaxel Content (µg)
H74939294600470	6	40	40	0	75	4.0 - 5.0	135
H74939294600670	6	60	60	1	75		207
H74939294600870	6	80	79	-1	75		272
H74939294601070	6	100	100	0	75		344
H74939294601270	6	120	119	-1	75		409
H74939294601570	6	150	149	-1	75		517
H74939294600410	6	40	40	0	130		135
H74939294600610	6	60	60	1	130		207
H74939294600810	6	80	79	-1	130		272
H74939294601010	6	100	100	0	130		344
H74939294601210	6	120	119	-1	130		409
H74939294601510	6	150	149	-1	130		517
H74939294700470	7	40	41	1	75	5.0 - 6.0	135
H74939294700670	7	60	60	0	75		207
H74939294700870	7	80	77	-3	75		272
H74939294701070	7	100	100	0	75		344
H74939294701270	7	120	118	-2	75		409
H74939294701570	7	150	149	0	75		517
H74939294700410	7	40	41	1	130		135
H74939294700610	7	60	60	0	130		207
H74939294700810	7	80	77	-3	130		272
H74939294701010	7	100	100	0	130		344
H74939294701210	7	120	118	-2	130		409
H74939294701510	7	150	149	0	130		517

3. INTENDED USE / INDICATIONS FOR USE

The ELUVIA Drug-Eluting Vascular Stent System is indicated for improving luminal diameter in the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery with reference vessel diameters (RVD) ranging from 4.0 mm - 6.0 mm and total lesion lengths up to 190 mm.

4. CONTRAINDICATIONS

- Women who are pregnant, breastfeeding, or plan to become pregnant in the next 5 years should not receive an ELUVIA Drug-Eluting Stent. It is unknown whether paclitaxel will be excreted in human milk, and there is a potential for adverse reaction in nursing infants from paclitaxel exposure.
- Patients who cannot receive recommended anti-platelet and /or anti-coagulant therapy.
- Patients judged to have a lesion that prevents proper placement of the stent or stent delivery system.

5. WARNINGS

Also see Section 1. WARNING Statement.

5.1 General

- The delivery system is not designed for use with power injection systems.
- Do not use a kinked delivery system.
- Only advance the stent delivery system over a guidewire.

- When catheters are in the vasculature, they should be manipulated only under fluoroscopy.
- Should another stent be needed, stents used should be of similar composition and allow for at least 5 mm of stent overlap.
- The stent delivery system is not intended for arterial blood monitoring.
- Prior to completion of the procedure, utilize fluoroscopy to ensure proper positioning of the stent. If the lesion is not fully covered, use additional stents as necessary to adequately treat the lesion.
- The minimally acceptable introducer or guide sheath size is printed on the package label. Do not attempt to pass the stent delivery system through a smaller size introducer or guide sheath than indicated on the label.
- In the event of thrombosis of the expanded stent, thrombolysis and/or PTA should be considered.
- In the event of complications such as infection, pseudoaneurysm or fistula formation, surgical removal of the stent may be required.
- Recrossing a partially or fully expanded deployed stent with adjunct devices must be performed with extreme caution to ensure that the adjunct device does not get caught within previously placed stent struts.
- Do not remove the thumbwheel lock prior to deployment. Premature removal of the thumbwheel lock may result in an unintended deployment of the stent.

5.2 Pre- and Post-Procedure Antiplatelet Therapy

It is strongly advised that the treating physician follow the Inter-Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy pre-procedure to reduce the risk of thrombosis. Post-procedure dual antiplatelet therapy is required for a minimum of 60 days.

Patients who require premature discontinuation of antiplatelet therapy due to significant active bleeding or the expectation of significant active bleeding should be monitored carefully for cardiovascular and thromboembolic events and once stabilized have their antiplatelet therapy restarted without unnecessary delay.

6. PRECAUTIONS

6.1 General Precautions

Only physicians who are familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with superficial femoral and/or proximal popliteal artery interventional procedures should use this device.

- Do not use after the "Use By" date specified on the package. See **HOW SUPPLIED** section prior to use.
- Stenting across a bifurcation or side branch could compromise future diagnostic or therapeutic procedures.
- The stent is not designed for repositioning.
- Once the stent is partially deployed, it cannot be "recaptured" or "reconstrained" using the stent delivery system.
- As with any type of intravascular implant, infection secondary to contamination of the stent may lead to complications such as thrombosis, pseudoaneurysm, or rupture.
- The stent may cause embolization from the site of the implant down the arterial lumen.
- This product should not be used in patients with uncorrected bleeding disorders or patients who cannot receive anticoagulation or antiplatelet aggregation therapy.
- Persons with a known hypersensitivity to paclitaxel (or structurally-related compounds), to the polymer or its individual component (see details in **Primer Polymer and Drug Matrix Copolymer Carrier** section), nickel, or titanium may suffer an allergic response to this implant.
- Persons with poor kidney function may not be good candidates for stenting procedures.
- Do not use if the temperature exposure indicator dot on the pouch label is red, indicating that the stent expansion may have been compromised.
- Do not use if the temperature exposure indicator dot on the pouch label is missing.
- Do not expose to organic solvents (e.g. alcohol).
- The safety and effectiveness of the coated device has not been established, or is unknown, in vascular regions other than those specifically indicated.

6.2 Pregnancy / Lactation

This product has not been tested in pregnant women or in men intending to father children; effects on the developing fetus have not been studied.

The risks and reproductive effects remain unknown.

It is not recommended that the ELUVIA Drug-Eluting Vascular Stent System be used in women attempting to conceive or who are pregnant.

It is not known whether paclitaxel is distributed in human milk. In lactating rats, milk concentrations appeared to be higher than maternal plasma levels and declined in parallel with the maternal levels. Mothers should be advised of the potential for serious adverse reactions to paclitaxel in nursing infants. Prior to implantation of an ELUVIA Drug-Eluting Vascular Stent, careful consideration should be given to the continuation of breast feeding, taking into account the importance of the stent to the mother.

6.3 Drug Information

The mechanism of action by which a Paclitaxel-Eluting Stent reduces or reverses neointima formation and proliferation, leading to restenosis, as demonstrated in clinical studies has not been established. It is known that paclitaxel promotes the assembly of microtubules from tubulin dimers and stabilizes microtubules by preventing depolymerization.

This stability results in the inhibition of the normal dynamic reorganization of the microtubule network that is essential for vital interphase and mitotic cellular functions.

6.4 Drug Interaction

Possible interactions of paclitaxel with concomitantly administered medications have not been formally investigated. Drug interactions of systemic chemotherapeutic levels of paclitaxel with possible concomitant medications are outlined in the labeling for finished pharmaceuticals containing paclitaxel, such as TAXOL. Given that the amount of paclitaxel loaded onto each ELUVIA Drug-Eluting Vascular Stent is at a minimum 400 times lower than that used in oncological applications of the drug and is released at considerably lower levels than this, drug interactions are unlikely to be detectable. This is reinforced since systemic levels of paclitaxel have not been detected post stent placement in clinical trials.

6.5 Magnetic Resonance Imaging (MRI)

A patient with this device can be scanned safely only under specific conditions. Failure to follow the conditions may result in severe injury.

Non-clinical testing has demonstrated the ELUVIA Stents are MR Conditional for single stents up to 150 mm and overlapping lengths up to 200 mm. A patient with this stent can be scanned safely, immediately after placement, under the following conditions:

- Static magnetic field of 1.5 Tesla or 3.0 Tesla
- Highest spatial gradient magnetic field of 40 Tesla/m (4,000 Gauss/cm) or less
- Maximum MR system reported whole body averaged specific absorption rate (SAR) of
  - ≤ 2 W/kg for landmarks (i.e. center of RF coil) above the umbilicus
  - ≤ 1 W/kg for landmarks below the umbilicus and above mid-thigh
  - ≤ 0.5 W/kg for landmarks below the mid-thigh

RF Heating

Under the scan conditions defined above, the ELUVIA Stent is expected to produce a maximum in-vivo temperature rise of 4 °C after 15 minutes of continuous scanning.

A 5 minute cool down period is recommended after scanning continuously at the maximum permissible SAR.

Image Artifact

In non-clinical testing, the image artifact caused by the device extends approximately 12 mm from the stent when imaged with a gradient echo pulse sequence and a 3 Tesla MRI system. The artifact does obscure the device lumen.

Recommendations

It is recommended that patients register the conditions under which the implant can safely be scanned with the MedicAlert Foundation (www.medicalert.org) or an equivalent organization.

6.6 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been performed to evaluate the carcinogenic potential of paclitaxel. Paclitaxel interacts with microtubules; this is the major mechanism by which it inhibits cell growth. One consequence is the loss of whole chromosomes via interactions with spindle microtubules during cell division. As such, paclitaxel is defined as an aneugen (agent causing an alteration in chromosome number). This indirect action is consistent with positive responses in *in vitro* and *in vivo* micronucleus genotoxicity assays, which detect DNA fragments. Positive results have also been reported for chromosomal aberrations in primary human lymphocytes. It is not known whether paclitaxel has a separate direct action on DNA in the generation of DNA strand breaks or fragments. It is negative in assays for gene mutation, including salmonella and CHO/HPRT. Paclitaxel administered via IV prior to and during mating produced impairment of fertility in male and female rats at doses > 1 mg/kg (approximately 19 times the dose provided by the largest ELUVIA Drug-Eluting Vascular Stent coated with 517 µg paclitaxel adjusted for body surface area).

7. POTENTIAL ADVERSE EVENTS

Potential adverse events which may be associated with the use of a peripheral stent include but are not limited to:

- Allergic reaction (to drug/polymer, contrast, device or other)
- Amputation
- Arterial aneurysm
- Arteriovenous fistula
- Death
- Embolization (air, plaque, thrombus, device, tissue, or other)
- Hematoma
- Hemorrhage (bleeding)
- Infection/Sepsis
- Ischemia
- Need for urgent intervention or surgery
- Pseudoaneurysm formation
- Renal insufficiency or failure
- Restenosis of stented artery
- Thrombosis/thrombus
- Transient hemodynamic instability (hypotensive/hypertensive episodes)
- Vasospasm
- Vessel injury, including perforation, trauma, rupture and dissection
- Vessel occlusion

Potential adverse effects not captured above that may be unique to the paclitaxel drug coating:

- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds) or the polymer stent coating (or its individual components)
- Alopecia
- Anemia
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/Arthralgia
- Peripheral neuropathy

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

8. CLINICAL STUDIES

8.1 Late Mortality Signal for Paclitaxel-Coated Devices

A meta-analysis of randomized controlled trials published in December 2018 by Katsanos et. al. identified an increased risk of late mortality at 2 years and beyond for paclitaxel-coated balloons and paclitaxel-eluting stents used to treat femoropopliteal arterial disease. In response to these data, FDA performed a patient-level meta-analysis of long-term follow-up data from the pivotal premarket randomized trials of paclitaxel-coated devices used to treat femoropopliteal disease using available clinical data through May 2019. The meta-analysis also showed a late mortality signal in study subjects treated with paclitaxel-coated devices compared to patients treated with uncoated devices. Specifically, in the 3 randomized trials with a total of 1090 patients and available 5-year data, the crude mortality rate was 19.8 % (range 15.9 % - 23.4 %) in patients treated with paclitaxel-coated devices compared to 12.7 % (range 11.2 % - 14.0 %) in subjects treated with uncoated devices. The relative risk for increased mortality at 5 years was 1.57 (95 % confidence interval 1.16 - 2.13), which corresponds to a 57 % relative increase in mortality in patients treated with paclitaxel-coated devices. As presented at the June 2019 FDA Advisory Committee Meeting, an independent meta-analysis of similar patient-level data provided by VIVA Physicians, a vascular medicine organization, reported similar findings with a hazard ratio of 1.38 (95 % confidence interval 1.06 - 1.80). Additional analyses have been conducted and are underway that are specifically designed to assess the relationship of mortality to paclitaxel-coated devices.

The presence and magnitude of the late mortality risk should be interpreted with caution because of multiple limitations in the available data, including wide confidence intervals due to a small sample size, pooling of studies of different paclitaxel-coated devices that were not intended to be combined, substantial amounts of missing study data, no clear evidence of a paclitaxel dose effect on mortality, and no identified pathophysiologic mechanism for the late deaths.

Paclitaxel-coated balloons and stents improve blood flow to the legs and decrease the likelihood of repeat procedures to reopen blocked blood vessels compared to uncoated devices. The benefits of paclitaxel-coated devices (e.g., reduced reinterventions) should be considered in individual patients along with potential risks (e.g., late mortality).

In the IMPERIAL Trial, Kaplan Meier mortality estimates at 2 years are 7.1 % (95 % CI: 4.1 %, 10.0 %) for the ELUVIA treatment device and 8.0 % (95 % CI: 3.7 %, 12.4 %) for the Zilver PTX paclitaxel-coated control device. Additional information regarding IMPERIAL Trial outcomes can be found in Section 8.2.

8.2 The IMPERIAL Trial

The clinical evidence supporting the safety and effectiveness of the ELUVIA Drug-Eluting Vascular Stent System for the treatment of symptomatic de-novo or restenotic lesions in the native superficial femoral artery (SFA) and/or proximal popliteal artery (PPA) with reference vessel diameters (RVD) ranging from 4.0 mm - 6.0 mm is from the IMPERIAL Trial.

A study titled "A randomized trial comparing the ELUVIA Drug-Eluting Vascular Stent versus Zilver PTX stent for treatment of superficial femoral and/or proximal popliteal arteries" (IMPERIAL) was conducted. The IMPERIAL Trial is a global, prospective, multicenter, 2:1 randomized (ELUVIA vs Zilver PTX), controlled, single-blind, non-inferiority trial (RCT). It also includes a concurrent, non-blinded, non-randomized, single-arm, pharmacokinetic (PK) substudy and a concurrent, non-blinded, non-randomized, Long Lesion (LL) substudy.

The primary objective of the study was to determine whether the ELUVIA Drug-Eluting Vascular Stent System showed acceptable performance in long-term (12-month) safety rates and vessel patency when treating femoropopliteal lesions.

A total of 524 subjects were enrolled in the IMPERIAL Trial, including 465 subjects in the RCT, 13 subjects in the PK substudy and 50 subjects in the Long Lesion substudy. There were 4 subjects enrolled in both the PK and Long Lesion substudy. Subjects were enrolled at 65 centers located in the United States, Canada, Japan, New Zealand and Europe. Subject follow-up is ongoing and will extend for 5 years post index procedure.

Eligible subjects were 18 years or older, and consented to participate in the study. These subjects had documented peripheral artery disease defined as Rutherford categories 2, 3, or 4 and evidence of a stenotic, restenotic or occlusive lesion(s) located in the native SFA or PPA with a degree of stenosis ≥ 70 % by visual angiographic assessment. The vessel diameter was ≥ 4 mm and ≤ 6 mm and total lesion length (or series of lesions) was ≥ 30 mm and ≤ 140 mm (> 140 mm and ≤ 190 mm in the Long Lesion substudy). Lesions were located at least 3 cm above the inferior edge of the femur. Subject follow-up occurred at: 1 month, 6 months, 12 months, 2 years, 3 years, 4 years and 5 years after the index procedure. The first subject was enrolled on December 3, 2015. Enrollment completed on February 15, 2017. Data collected through April 4, 2018 is included below.

The primary study endpoints were as follows:

- The primary safety endpoint assessed the occurrence of Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization (TLR) through 12 months. This safety endpoint was designed to demonstrate that the 12-month MAE-free rate for the ELUVIA treatment group is non-inferior to the Zilver PTX control group.
- The RCT primary effectiveness endpoint assessed primary patency at 12 months post-procedure. This effectiveness endpoint was designed to demonstrate that the 12-month primary patency for the ELUVIA treatment group is non-inferior to the Zilver PTX control group. Primary vessel patency was defined as the percentage of lesions (target stented segments) that reached the endpoint without a hemodynamically significant stenosis on duplex ultrasound (DUS) (Peak Systolic Velocity Ratio {PSVR} is ≤ 2.4), and without clinically-driven TLR or bypass of the target lesion before or on the DUS follow-up visit.
- The LL substudy primary effectiveness endpoint assessed primary patency at 12 months post-procedure. There was a non-statistically driven performance goal (60 %) which was developed from the historical long stent performance of the Innova bare metal stent system and the expected enhanced performance (10 %) for the ELUVIA Stent System.

The IMPERIAL Trial employed independent duplex ultrasound, X-ray and angiographic core laboratories to review and analyze key study variables. An independent data reviewer was used to review study data on an ongoing basis and identify any potential safety trends. Adjudication of any potential major adverse events was conducted by an independent Clinical Events Committee (CEC).

Patient Population

Table 8-1 provides a review of baseline demographics and medical history of the 465 subjects enrolled into the IMPERIAL Randomized Controlled Trial (RCT). Table 8-2 provides a review of baseline demographics and medical history of the 50 subjects enrolled into the Long Lesion (LL) substudy.

Table 8-1. Baseline Demographics and Medical History - RCT (N=465)

Subject Characteristic	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Demographics		
Age (Year)	68.5 ± 9.5 (309) (39.0, 90.0)	67.8 ± 9.4 (156) (38.0, 87.0)
Male Gender	66.0 % (204 / 309)	66.7 % (104 / 156)
Race/Ethnicity[1]		
Hispanic or Latino	5.8 % (18 / 309)	3.8 % (6 / 156)
Caucasian	66.3 % (205 / 309)	69.2% (108 / 156)
Asian	18.4 % (57 / 309)	17.9 % (28 / 156)
Japanese	18.1 % (56 / 309)	17.9 % (28 / 156)
Black, or African heritage	6.8 % (21 / 309)	7.1 % (11 / 156)
Native Hawaiian or other Pacific Islander	0.3 % (1 / 309)	0.0 % (0 / 156)
American Indian or Alaska Native	0.6 % (2 / 309)	1.3 % (2 / 156)
Other	1.0 % (3 / 309)	0.6 % (1 / 156)
Not Disclosed	0.6 % (2 / 309)	0.0 % (0 / 156)
General Medical History		
History of Smoking		
Current	35.3 % (109 / 309)	40.4 % (63 / 156)
Previous	50.8 % (157 / 309)	43.6 % (68 / 156)
Never	13.6 % (42 / 309)	14.1 % (22 / 156)
Unknown	0.3 % (1 / 309)	1.9 % (3 / 156)
Current Diabetes Mellitus	41.7 % (129 / 309)	43.6 % (68 / 156)
Type 1	2.3 % (3 / 129)	4.4 % (3 / 68)

Subject Characteristic	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Type 2	92.2 % (119 / 129)	94.1 % (64 / 68)
Unknown	5.4 % (7/ 129)	1.5 % (1 / 68)
Current Method of Treatment		
Diet	31.0 % (40 / 129)	25.0 % (17 / 68)
Diet (only)	9.3 % (12 / 129)	4.4 % (3 / 68)
Medically Treated	89.9 % (116 / 129)	94.1 % (64 / 68)
Oral Agent	72.1 % (93 / 129)	75.0 % (51 / 68)
Insulin	38.0 % (49 / 129)	38.2 % (26 / 68)
Other	1.6 % (2 / 129)	0.0 % (0 / 68)
Unknown	0.8 % (1 / 129)	1.5 % (1 / 68)
History of Hyperlipidemia requiring medication	76.3 % (235 / 308)	75.6 % (118 / 156)
History of Hypertension requiring medication	82.2 % (254 / 309)	85.3 % (133 / 156)
History of Chronic Obstructive Pulmonary Disease	15.6 % (48 / 308)	18.1 % (28 / 155)
Cardiac History		
History of Coronary Artery Disease	50.8 % (156 / 307)	45.2 % (70 / 155)
History of Myocardial Infarction (MI)	19.6 % (60 / 306)	17.5 % (27 / 154)
History of Congestive Heart Failure	8.5 % (26 / 307)	7.8 % (12 / 154)
New York Heart Assoc. (NYHA) Classification		
I	19.2 % (5 / 26)	25.0 % (3 / 12)
II	23.1 % (6 / 26)	41.7 % (5 / 12)
III	15.4 % (4 / 26)	8.3 % (1 / 12)
IV	0.0 % (0 / 26)	0.0 % (0 / 12)
Unknown	42.3 % (11 / 26)	25.0 % (3 / 12)
History of Percutaneous Coronary Intervention (PCI)	32.5 % (100 / 308)	34.2 % (53 / 155)
History of Coronary Artery Bypass Graft (CABG) Surgery	14.0 % (43 / 308)	13.5 % (21 / 156)
Current Anginal Status		
Stable Angina	10.4 % (32 / 309)	12.2 % (19 / 156)
Unstable Angina	0.0 % (0 / 309)	0.0 % (0 / 156)
None	86.7 % (268 / 309)	86.5 % (135 /1 56)
Unknown	2.9 % (9 / 309)	1.3 % (2 / 156)
Neurologic/Renal History		
History of Transient Ischemic Attacks (TIA)	4.5% (14/308)	3.9% (6/155)
History of Cerebrovascular Accident (CVA)	9.7% (30/309)	9.0% (14/156)
History of Renal Insufficiency	8.1% (25/309)	7.1% (11/156)
History of Renal Percutaneous Intervention	1.9% (6/309)	0.6% (1/155)
Peripheral Vascular History		
History of Peripheral Vascular Surgery	12.9 % (40 / 309)	9.6 % (15 / 156)
History of Endovascular Interventions in Target Vessel	8.7 % (27 / 309)	11.0 % (17 / 155)
Type of Interventions		
Atherectomy	1.3 % (4 / 309)	3.2 % (5 / 156)
Drug Coated Balloon	2.6 % (8 / 309)	1.9 % (3 / 156)

Subject Characteristic	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Percutaneous Transluminal Angioplasty (PTA)	6.1 % (19 / 309)	7.7 % (12 / 156)
Stenting	0.6 % (2 / 309)	0.0 % (0 / 156)
Other	1.0 % (3 / 309)	1.9 % (3 / 156)
History of Other Peripheral Endovascular Interventions (other than Target Vessel)	36.2 % (112 / 309)	31.6 % (49 / 155)
Type of Most Recent Intervention		
Atherectomy	8.4 % (26 / 309)	7.7 % (12 / 156)
Drug Coated Balloon	9.4 % (29 / 309)	7.7 % (12 / 156)
Percutaneous Transluminal Angioplasty (PTA)	16.8 % (52 / 309)	12.8 % (20 / 156)
Stenting	23.9 % (74 / 309)	21.8 % (34 / 156)
Other	0.6 % (2 / 309)	2.6 % (4 / 156)
History of Claudication	98.4 % (303 / 308)	97.4 % (151 / 155)

[1]Subjects that are having more than one race will be considered only once in the sub category where less number of subjects are available. For example, if a subject has races ticked as "Caucasian" and "Hispanic or Latino" will be considered in "Hispanic or Latino" as this sub category has less number of subjects.

Table 8-2. Baseline Demographics and Medical History - LL (N=50)

Subject Characteristic	ELUVIA N = 50 Subjects
Demographics	
Age (Year)	68.2 ± 8.9 (50) (51.0, 84.0)
Male Gender	64.0 % (32 / 50)
Race/Ethnicity[1]	
Hispanic or Latino	6.0 % (3 / 50)
Caucasian	60.0 % (30 / 50)
Asian	22.0 % (11 / 50)
Japanese	22.0 % (11 / 50)
Black, or African heritage	12.0 % (6 / 50)
Native Hawaiian or other Pacific Islander	0.0 % (0 / 50)
American Indian or Alaska Native	0.0 % (0 / 50)
Other	0.0 % (0 / 50)
Not Disclosed	0.0 % (0 / 50)
General Medical History	
History of Smoking	
Current	32.0 % (16 / 50)
Previous	52.0 % (26 / 50)
Never	16.0 % (8 / 50)
Unknown	0.0 % (0 / 50)
Current Diabetes Mellitus	40.0 % (20 / 50)
Type 1	5.0 % (1 / 20)
Type 2	90.0 % (18 / 20)
Unknown	5.0 % (1 / 20)
Current Method of Treatment	
Diet	20.0 % (4 / 20)
Diet (only)	5.0 % (1 / 20)
Medically Treated	95.0 % (19 / 20)

Subject Characteristic	ELUVIA N = 50 Subjects
Oral Agent	85.0 % (17 / 20)
Insulin	40.0 % (8 / 20)
Other	0.0 % (0 / 20)
Unknown	0.0 % (0 / 20)
History of Hyperlipidemia requiring medication	82.0 % (41 / 50)
History of Hypertension requiring medication	92.0 % (46 / 50)
History of Chronic Obstructive Pulmonary Disease	18.0 % (9 / 50)
Cardiac History	
History of Coronary Artery Disease	56.0 % (28 / 50)
History of Myocardial Infarction (MI)	18.0 % (9 / 50)
History of Congestive Heart Failure	16.0 % (8 / 50)
New York Heart Assoc. (NYHA) Classification	
I	25.0 % (2 / 8)
II	50.0 % (4 / 8)
III	0.0 % (0 / 8)
IV	0.0 % (0 / 8)
Unknown	25.0 % (2 / 8)
History of Percutaneous Coronary Intervention (PCI)	36.0 % (18 / 50)
History of Coronary Artery Bypass Graft (CABG) Surgery	14.3 % (7 / 49)
Current Anginal Status	
Stable Angina	10.0 % (5 / 50)
Unstable Angina	0.0 % (0 / 50)
None	88.0 % (44 / 50)
Unknown	2.0 % (1 / 50)
Neurologic/Renal History	
History of Transient Ischemic Attacks (TIA)	10.0 % (5 / 50)
History of Cerebrovascular Accident (CVA)	18.0 % (9 / 50)
History of Renal Insufficiency	6.0 % (3 / 50)
History of Renal Percutaneous Intervention	0.0 % (0 / 50)
Peripheral Vascular History	
History of Peripheral Vascular Surgery	4.0 % (2 / 50)
History of Endovascular Interventions in Target Vessel	4.0 % (2 / 50)
Type of Interventions	
Atherectomy	2.0 % (1 / 50)
Drug Coated Balloon	0.0 % (0 / 50)
Percutaneous Transluminal Angioplasty (PTA)	2.0 % (1 / 50)
Stenting	0.0 % (0 / 50)
Other	0.0 % (0 / 50)
History of Other Peripheral Endovascular Interventions (other than Target Vessel)	40.0 % (20 / 50)
Type of Most Recent Intervention	
Atherectomy	16.0 % (8 / 50)
Drug Coated Balloon	12.0 % (6 / 50)

Subject Characteristic	ELUVIA N = 50 Subjects
Percutaneous Transluminal Angioplasty (PTA)	26.0 % (13 / 50)
Stenting	26.0 % (13 / 50)
Other	0.0 % (0 / 50)
History of Claudication	98.0 % (49 / 50)

[1]Subjects that are having more than one race will be considered only once in the sub category where less number of subjects are available. For example, if a subject has races ticked as "Caucasian" and "Hispanic or Latino" will be considered in "Hispanic or Latino" as this sub category has less number of subjects.

Lesion Characteristics

Table 8-3 and **Table 8-4** present the baseline angiographic core lab reported lesion characteristics for the RCT and LL substudy, respectively.

Table 8-3. Baseline Angiographic Core Lab-Reported Lesion Characteristics - RCT (N=465)

	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Treated Limb		
Right leg	51.5 % (159 / 309)	55.1 % (86 / 156)
Left leg	48.5 % (150 / 309)	44.9 % (70 / 156)
Arterial Segments[a]		
Ostial	1.6 % (5 / 309)	0.6 % (1 / 156)
Proximal	12.9 % (40 / 309)	10.3 % (16 / 156)
Mid	65.0 % (201 / 309)	66.7 % (104 / 156)
Distal	66.3 % (205 / 309)	65.4 % (102 / 156)
Proximal Popliteal Artery	18.0 % (37 / 205)	12.7 % (13 / 102)
mm from Ostium (mm)	168.0 ± 73.4 (270) (0.0, 379.6)	168.5 ± 71.2 (126) (4.4, 343.1)
Length (mm)	86.5 ± 36.9 (308) (12.6, 171.3)	81.8 ± 37.3 (154) (12.6, 164.6)
Lesion Type		
Eccentric Lesion	66.9 % (206 / 308)	67.1 % (104 / 155)
Concentric Lesion	33.1 % (102 / 308)	32.9 % (51 / 155)
Bend (degrees)		
> 45 degrees	0.0 % (0 / 308)	0.0 % (0 / 155)
> 90 degrees	0.0 % (0 / 308)	0.0 % (0 / 155)
Thrombus[b]		
Grade 0	100.0 % (308 / 308)	100.0 % (155 / 155)
Grade 1	0.0 % (0 / 308)	0.0 % (0 / 155)
Grade 2	0.0 % (0 / 308)	0.0 % (0 / 155)
Grade 3	0.0 % (0 / 308)	0.0 % (0 / 155)
Grade 4	0.0 % (0 / 308)	0.0 % (0 / 155)
Grade 5	0.0 % (0 / 308)	0.0 % (0 / 155)
Calcification		
None/Mild	36.5 % (112 / 307)	32.3 % (50 / 155)
Moderate	22.8 % (70 / 307)	34.8 % (54 / 155)
Severe	40.1 % (123 / 307)	32.3 % (50 / 155)
Unknown	0.7 % (2 / 307)	0.6 % (1 / 155)
Ulceration (Present)	5.2 % (16 / 309)	2.6 % (4 / 156)
Aneurysm (Present)	0.0 % (0 / 309)	2.6 % (4 / 156)
Patency to Foot	94.8 % (293 / 309)	93.6 % (146 / 156)

	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Anterior Tibial Artery (Patent)	42.1 % (130 / 309)	47.4 % (74 / 156)
Posterior Tibial Artery	57.9 % (179 / 309)	60.9 % (95 / 156)
Peroneal Artery	71.5 % (221 / 309)	64.7 % (101 / 156)
Profunda Femoris Artery	83.2 % (257 / 309)	82.7 % (129 / 156)
% Diameter Stenosis	80.7 ± 16.5 (308) (30.4, 100.0)	80.8 ± 16.4 (155) (39.0, 100.0)
< 50 %	1.6 % (5 / 308)	1.9 % (3 / 155)
50 % - < 100 %	67.2 % (207 / 308)	67.7 % (105 / 155)
100 % (Occlusion)	31.2 % (96 / 308)	30.3 % (47 / 155)

[a] Subjects under "Arterial Segments" may have checked more than one location present.
[b]Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100 %.

Table 8-4. Baseline Angiographic Core Lab Reported Lesion Characteristics - LL (N = 50)

	ELUVIA N = 50 Subjects
Treated Limb	
Right leg	64.0 % (32 / 50)
Left leg	36.0 % (18 / 50)
Arterial Segments[a]	
Ostial	2.0 % (1 / 50)
Proximal	54.0 % (27 / 50)
Mid	90.0 % (45 / 50)
Distal	76.0 % (38 / 50)
Proximal Popliteal Artery	18.4 % (7 / 38)
mm from Ostium (mm)	93.5 ± 58.6 (46) (0.0, 260.5)
Length (mm)	162.8 ± 34.7 (49) (55.6, 243.8)
Lesion Type	
Eccentric Lesion	64.0 % (32 / 50)
Concentric Lesion	36.0 % (18 / 50)
Bend (degrees)	
> 45 degrees	0.0 % (0 / 50)
> 90 degrees	0.0 % (0 / 50)
Thrombus[b]	
Grade 0	100.0 % (50 / 50)
Grade 1	0.0 % (0 / 50)
Grade 2	0.0 % (0 / 50)
Grade 3	0.0 % (0 / 50)
Grade 4	0.0 % (0 / 50)
Grade 5	0.0 % (0 / 50)
Calcification	
None/Mild	28.0 % (14 / 50)
Moderate	42.0 % (21 / 50)
Severe	28.0 % (14 / 50)
Unknown	2.0 % (1 / 50)
Ulceration (Present)	8.0 % (4 / 50)
Aneurysm (Present)	2.0 % (1 / 50)

	ELUVIA N = 50 Subjects
Patency to Foot	100.0 % (50 / 50)
Anterior Tibial Artery (Patent)	40.0 % (20 / 50)
Posterior Tibial Artery	56.0 % (28 / 50)
Peroneal Artery	72.0 % (36 / 50)
Profunda Femoris Artery	86.0 % (43 / 50)
% Diameter Stenosis	81.9 ± 15.0 (50) (49.8, 100.0)
< 50 %	2.0 % (1 / 50)
50 % - < 100 %	66.0 % (33 / 50)
100 % (Occlusion)	32.0 % (16 / 50)

[a]Subjects under "Arterial Segments" may have checked more than one location present.
[b]Thrombus could have subjects with "N/A" response as allowed by CRF so percentages may not add up to 100 %.

Study Results

Primary Effectiveness Results - RCT

Primary patency at 12 months was determined to be 86.8 % in the treatment group (ELUVIA) and 81.5 % in the control group (Zilver PTX), with the one-sided lower 95 % confidence bound of - 0.66 % on the difference between the treatment groups being greater than - 10 % (non-inferiority p-value < .0001). Therefore, the primary effectiveness endpoint was met and ELUVIA is concluded to be non-inferior to Zilver PTX for device effectiveness.

Table 8-5. Primary Effectiveness Endpoints - RCT

Intent-To-Treat (N = 421 Subjects)	ELUVIA N = 280 Subjects	Zilver PTX N = 141 Subjects	Difference [95 % CI]	One-sided 95 % Farrington-Manning Lower Confidence Bound	Non-Inferiority Margin (Delta)	Non-Inferiority P-value
12 - Month Primary Patency[1]	86.8 % (231 / 266)	81.5 % (106 / 130)	5.3 % [- 2.5 %, 13.1 %]	- 0.66 %	- 10 %	< .0001

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS FU visit.
P-value is from the Farrington-Manning test and is based on the standard normal distribution.
A two-group Farrington-Manning test is used to test the one-sided hypothesis of non-inferiority in proportions. If the P-value from the one-sided Farrington-Manning test is < 0.05, ELUVIA is concluded to be non-inferior to Zilver PTX.

Table 8-6 presents vessel patency through 12 months for all evaluable subjects in the full cohort of the RCT group.

Primary patency at 12 months was determined to be 86.8 % in the treatment group (ELUVIA) and 77.5 % in the control group (Zilver PTX).

Table 8-6. Vessel Patency Analysis through 12 Months - Full Cohort RCT (N=465)

	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Patency at 6 Months		
Primary Patency[1]	94.5 % (274 / 290)	91.2 % (135 / 148)
Assisted Primary Patency[2]	96.5 % (274 / 284)	95.2 % (138 / 145)
Patency at 12 Months		
Primary Patency[1]	86.8 % (243 / 280)	77.5 % (110 / 142)
Assisted Primary Patency[2]	92.9 % (249 / 268)	86.9 % (119 / 137)

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS FU visit.
[2]Assisted Primary Patency: percentage (%) of lesions (target stented segments) without clinically-driven TLR and those with clinically-driven TLR (not due to complete occlusion or by-pass) that reach endpoint without restenosis.
The subjects with available diagnostic DUS images are included for the analysis.

Safety Endpoint Results - RCT

The MAE-free rate at 12 months was determined to be 94.9 % in the treatment group (ELUVIA) and 91.0 % in the control group (Zilver PTX), with the one-sided lower 95 % confidence bound of - 0.46 % on the difference between the treatment groups being greater than - 10 % (non-inferiority p-value < .0001). Therefore, the primary safety endpoint was met and ELUVIA is concluded to be non-inferior to Zilver PTX for device safety.

Table 8-7. Primary Safety Endpoints - RCT

Intent-To-Treat (N = 421 Subjects)	ELUVIA N = 280 Subjects	Zilver PTX N = 141 Subjects	Difference [95 % CI]	One-sided 95 % Farrington-Manning Lower Confidence Bound	Non-Inferiority Margin (Delta)	Non-Inferiority P-value
12 - Month MAE[1]-Free	94.9 % (259 / 273)	91.0 % (121 / 133)	3.9 % [- 1.6 %, 9.4 %]	- 0.46 %	- 10 %	< .0001

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.
P-value is from the Farrington-Manning test and is based on the standard normal distribution.
A two-group Farrington-Manning test is used to test the one-sided hypothesis of non-inferiority in proportions. If the P-value from the one-sided Farrington-Manning test is < 0.05, ELUVIA is concluded to be non-inferior to Zilver PTX.

Table 8-8 shows the individual components of the primary safety endpoint: all causes of death through 1 month, target limb major amputation through 12 months and target lesion revascularization (TLR) through 12 months. The rate of TLR at 12 months was 4.5 % in the treatment group (ELUVIA) and 9.0 % in the control group (Zilver PTX). One major amputation occurred in the treatment group (ELUVIA).

Table 8-8. Safety Endpoints through 12 Months - Full Cohort RCT (N=465)

	ELUVIA N = 309 Subjects	Zilver PTX N = 156 Subjects
Primary Safety Endpoint		
12 - Month MAE[1]-Free	95.1 % (273 / 287)	91.0 % (132 / 145)
12 - Month MAE[1] and Components		
12 - Month MAE[1] (Composite Endpoint)	4.9 % (14 / 287)	9.0 % (13 / 145)
All Causes of Deaths at 1 Month	0.0 % (0 / 287)	0.0 % (0 / 145)
Target Limb Major Amputation	0.3 % (1 / 287)	0.0 % (0 / 145)
Target Lesion Revascularization	4.5 % (13 / 287)	9.0 % (13 / 145)
Clinically-Driven	4.5 % (13 / 287)	9.0 % (13 / 145)
Non-Clinically-Driven	0.0 % (0 / 287)	0.0 % (0 / 145)

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.

Evaluation of Safety

Table 8-9 displays the rates of site-reported Serious Adverse Events (SAEs) reported by MedDRA System Organ Class (SOC) for the RCT.

Table 8-9. Frequency of Site-Reported Serious Adverse Events to 12 Months - Full Cohort RCT (N=465)

Serious Adverse Event		ELUVIA (N = 309 Subjects)		Zilver PTX (N = 156 Subjects)	
MedDRA System Organ Class	MedDRA Preferred Term	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Total	Total	242	41.4 % (128 / 309)	140	42.3 % (66 / 156)
Vascular disorders	Total	93	22.3 % (69 / 309)	55	25.0 % (39 / 156)
Cardiac disorders	Total	32	7.4 % (23 / 309)	20	9.6 % (15 / 156)
Infections and infestations	Total	18	3.9 % (12 / 309)	21	8.3 % (13 / 156)
Musculoskeletal and connective tissue disorders	Total	14	4.2 % (13 / 309)	7	3.8 % (6 / 156)
Gastrointestinal disorders	Total	14	3.9 % (12 / 309)	3	1.9 % (3 / 156)
Nervous system disorders	Total	12	3.6 % (11 / 309)	7	3.8 % (6 / 156)
Respiratory, thoracic and mediastinal disorders	Total	10	2.6 % (8 / 309)	4	2.6 % (4 / 156)
Injury, poisoning and procedural complications	Total	9	2.6 % (8 / 309)	7	4.5 % (7 / 156)
General disorders and administration site conditions	Total	9	1.9 % (6 / 309)	4	2.6 % (4 / 156)
Blood and lymphatic system disorders	Total	9	2.3 % (7 / 309)	0	0.0 % (0 / 156)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	Total	7	1.9 % (6 / 309)	3	1.9 % (3 / 156)
Skin and subcutaneous tissue disorders	Total	3	1.0 % (3 / 309)	2	1.3 % (2 / 156)
Renal and urinary disorders	Total	3	1.0 % (3 / 309)	1	0.6 % (1 / 156)
Endocrine disorders	Total	3	1.0 % (3 / 309)	0	0.0 % (0 / 156)
Metabolism and nutrition disorders	Total	2	0.6 % (2 / 309)	2	1.3 % (2 / 156)
Psychiatric disorders	Total	1	0.3 % (1 / 309)	2	0.6 % (1 / 156)
Ear and labyrinth disorders	Total	1	0.3 % (1 / 309)	1	0.6 % (1 / 156)
Eye disorders	Total	1	0.3 % (1 / 309)	1	0.6% (1 / 156)
Reproductive system and breast disorders	Total	1	0.3 % (1 / 309)	0	0.0 % (0 / 156)

"Events" numbers are total episodes of each type of event among all subjects.
"Rate of Subjects with Event" numbers are percent of subjects who experienced one or more episodes of the event.
"Events" numbers for "TOTAL" are the sum of the individual event category totals.
"Rate of Subjects with Event" numbers for "TOTAL" is the percent of subjects who experienced an adverse event.

Secondary Endpoints

Full cohort analysis of secondary endpoints for procedural/technical success, MAE rate at 1 month, non-serious non-device/procedure-related AE rates, rate of primary and secondary sustained clinical improvement as assessed by changes in Rutherford Classification from baseline, rate of hemodynamic improvement as assessed by changes in Ankle-Brachial Index (ABI), walking improvement and patient utility values assessed by change in Walking Impairment Questionnaire and EQ-5D, fracture rate, distribution of Rutherford Classification during follow-up as compared to baseline, rate of hemodynamic improvement as assessed by changes in Ankle-Brachial Index (ABI) from baseline, Walking Improvement at 12 months assessed by change in Six Minute Hall Walk (6 MHW) from baseline, changes in healthcare utilization over time, and PK parameters calculated for subjects in the PK substudy were observational and demonstrated similar outcomes in both treatment arms.

Primary Effectiveness and Safety Endpoint Results – LL

Table 8-10 presents the primary effectiveness endpoint results for the LL Substudy. Primary patency at 12 months was determined to be 87.0 %.

Table 8-10. Vessel Patency Analysis through 12 Months - LL (N=50)

	ELUVIA N = 50 Subjects
Patency at 6 Months	
Primary Patency[1]	93.9 % (46 / 49)
Assisted Primary Patency[2]	97.9 % (47 / 48)
Patency at 12 Months	
Primary Patency[1]	87.0 % (40 / 46)
Assisted Primary Patency[2]	93.3 % (42 / 45)

[1]Primary Patency: percentage (%) of lesions (target stented segments) that reach endpoint without a hemodynamically significant stenosis on DUS and without clinically-driven TLR or, bypass of the target lesion before or on the DUS FU visit.
[2]Assisted Primary Patency: percentage (%) of lesions (target stented segments) without clinically-driven TLR and those with clinically-driven TLR (not due to complete occlusion or bypass) that reach endpoint without restenosis.

Table 8-11 presents the primary safety endpoint and individual components for the LL substudy. The 93.5 % MAE-free rate observed in the LL substudy is similar to the 94.9 % MAE-free rate observed in the treatment group (ELUVIA) in the RCT. The composite rate of MAEs was 6.5 %. The only MAEs that occurred in the LL substudy were TLRs; there were no deaths or major amputations.

Table 8-11. Safety Endpoints through 12 Months - LL (N=50)

	ELUVIA N = 50 Subjects
Primary Safety Endpoint	
12 - Month MAE[1]-Free	93.5 % (43 / 46)
12 - Month MAE[1] and Components	
12 - Month MAE[1] (Composite Endpoint)	6.5 % (3 / 46)
All Causes of Deaths at 1 Month	0.0 % (0 / 46)
Target Limb Major Amputation	0.0 % (0 / 46)
Target Lesion Revascularization	6.5 % (3 / 46)
Clinically-Driven	6.5 % (3 / 46)
Non-Clinically-Driven	0.0 % (0 / 46)

[1]Twelve-Month Major Adverse Events (MAEs) defined as all causes of death through 1 month, target limb major amputation through 12 months and/or target lesion revascularization through 12 months.

Evaluation of Safety

Table 8-12 displays the rates of site-reported Serious Adverse Events (SAEs) reported by MedDRA System Organ Class (SOC) for the LL substudy.

Table 8-12. Frequency of Site-Reported Serious Adverse Events to 12 Months - LL (N=50)

Serious Adverse Event		ELUVIA (N = 50 Subjects)	
MedDRA System Organ Class	**MedDRA Preferred Term**	**Events**	**Rate of Subjects with Event**
Total	Total	26	30.0 % (15 / 50)
Vascular disorders	Total	8	14.0 % (7 / 50)
Cardiac disorders	Total	5	10.0 % (5 / 50)
Gastrointestinal disorders	Total	5	6.0 % (3 / 50)
Infections and infestations	Total	2	4.0 % (2 / 50)
Injury, poisoning and procedural complications	Total	2	2.0 % (1 / 50)
Blood and lymphatic system disorders	Total	1	2.0 % (1 / 50)
General disorders and administration site conditions	Total	1	2.0 % (1 / 50)
Nervous system disorders	Total	1	2.0 % (1 / 50)
Respiratory, thoracic and mediastinal disorders	Total	1	2.0 % (1 / 50)

"Events" numbers are total episodes of each type of event among all subjects.
"Rate of Subjects with Event" numbers are percent of subjects who experienced one or more episodes of the event.
"Events" numbers for "TOTAL" are the sum of the individual event category totals.
"Rate of Subjects with Event" numbers for "TOTAL" is the percent of subjects who experienced an adverse event.

Table 8-13 presents the primary patency and MAE rates grouped by lesion length tertiles.

Table 8-13. 12-Month Vessel Patency and MAE Rates for Lesion Length Tertiles

Lesion Length Tertiles	ELUVIA ALL (N = 50)	ELUVIA T1 (N = 13)	ELUVIA T2 (N = 15)	ELUVIA T3 (N = 22)
12 - Month Primary Patency	87.0 % (40 / 46) [73.7 %, 95.1 %]	91.7 % (11 / 12)	86.7 % (13 / 15)	84.2 % (16 / 19)
12 - Month MAE-Free	93.5 % (43 / 46) [82.1 %, 98.6 %]	92.3 % (12 / 13)	92.9 % (13 / 14)	94.7 % (18 / 19)

T1:- "<= 150 mm"; T2:- " > 150 mm to <= 170 mm"; T3:- " > 170 mm".
Site reported lesion length is considered for analysis for the subject with missing core lab lesion length.

9. HOW SUPPLIED

The ELUVIA Drug-Eluting Vascular Stent System is supplied sterile inside a pouch. The device is sterilized via Ethylene Oxide. The device is non-pyrogenic.

Handling and Storage

Do not use if package is opened or damaged.

Do not use if labeling is incomplete or illegible.

Protect from light. Do not remove from carton until ready for use. Store at 25 °C (77 °F); excursions permitted to 15 °C - 30 °C (59 °F - 86 °F).

The ELUVIA Drug-Eluting Vascular Stent is a nitinol stent that has an upper temperature limit of 55 °C (131 °F).

Precaution: Do not use if the temperature indicator dot on the carton or pouch is red indicating that stent expansion may have been compromised.

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10. OPERATIONAL INSTRUCTIONS

10.1 Inspection Prior To Use

Check the pouch for "Use By" date. Carefully inspect the sterile pouch before opening. Do not use the product after the "Use By" date. If the integrity of the sterile package has been compromised prior to the product "Use By" date (e.g., damage of the package), contact your local Boston Scientific representative for return information. Do not use if any defects are noted.

10.2 Recommended Materials

- 0.035 in (0.89 mm) stiff guidewire of appropriate length (300 cm length recommended for 130 cm length stent delivery systems)
- Introducer or guide sheath of appropriate size and length and equipped hemostatic valve
- Luer lock syringe 10 ml (10 cc) for flushing the stent delivery system

10.3 Patient Preparation

The percutaneous placement of a self-expanding stent in a stenotic or obstructed artery should be done in an angiography procedure room with the appropriate imaging equipment. Patient preparation and sterile precautions should be the same as for any angioplasty procedure. Appropriate antiplatelet and anticoagulation therapy must be administered pre- and post-procedure in accordance with standard practices. Angiography should be performed to map out the extent of the lesion(s) and the collateral flow. Access vessels must be sufficiently patent to proceed with further intervention. If thrombus is present or suspected, thrombolysis should precede stent deployment using standard acceptable practice.

10.4 Inject Contrast Media

Perform angiogram using standard technique.

10.5 Evaluate and Mark the Stenosis

Observe fluoroscopically the most distal view of the stenotic or obstructed artery. Obtain a road map image of the lesion area if necessary.

10.6 Select Proper Stent System

1. Measure the diameter of the reference vessel (proximal and distal to the lesion or obstruction). Select a stent based on **Table 2-2**.
2. Measure the entire length of the actual lesion and select the proper length of the stent(s) to be deployed. To help ensure adequate apposition, it is recommended that the length of the stent be chosen so that the ends of the stent extend at least 5 mm beyond both ends of the lesion into healthy tissue.

   Should more than one stent be required to cover the lesion, allow for at least 5 mm of stent overlap. It is generally recommended that the distal stent be placed first.

   When multiple stents are required, if placement results in metal to metal contact, stent materials should be of similar composition.
3. Estimate the distance between the lesion and the entry site to select the proper stent delivery system length. The 75 cm working length device is recommended for ipsilateral approach.

10.7 Preparation of Stent Delivery System

1. Open the outer box to reveal the pouch containing the stent delivery system.
2. Check the temperature exposure indicator on the pouch label to confirm that the product has not been compromised. See **6.1 General Precautions** section.
3. After careful inspection of the pouch looking for damage to the sterile barrier, carefully peel open the pouch and extract the stent delivery system tray.
4. Carefully withdraw the stent delivery system from the tray by grasping the handle of the delivery system.
5. Examine the stent delivery system for any damage. If it is suspected that the sterility or integrity of the device has been compromised (i.e. kinking or missing component), the device should not be used. The device should not be used if the device is kinked, or if the thumbwheel lock is not attached.
6. Do not remove the thumbwheel lock ② prior to deployment. Premature removal of the thumbwheel lock may result in an unintended deployment of the stent.
7. Attach a 10 ml (10 cc) syringe filled with saline to the flushing luer ⑥ on the handle. Apply positive pressure. Continue to flush until saline appears at the distal end of the guidewire lumen. Remove the flushing luer ⑥ (by pulling the syringe or by pulling flushing luer ⑥) (Reference **Figure 4**).

10.8 Delivery Procedures

1. Gain arterial access utilizing a 6F (2.1 mm) or larger sheath with a hemostatic valve.

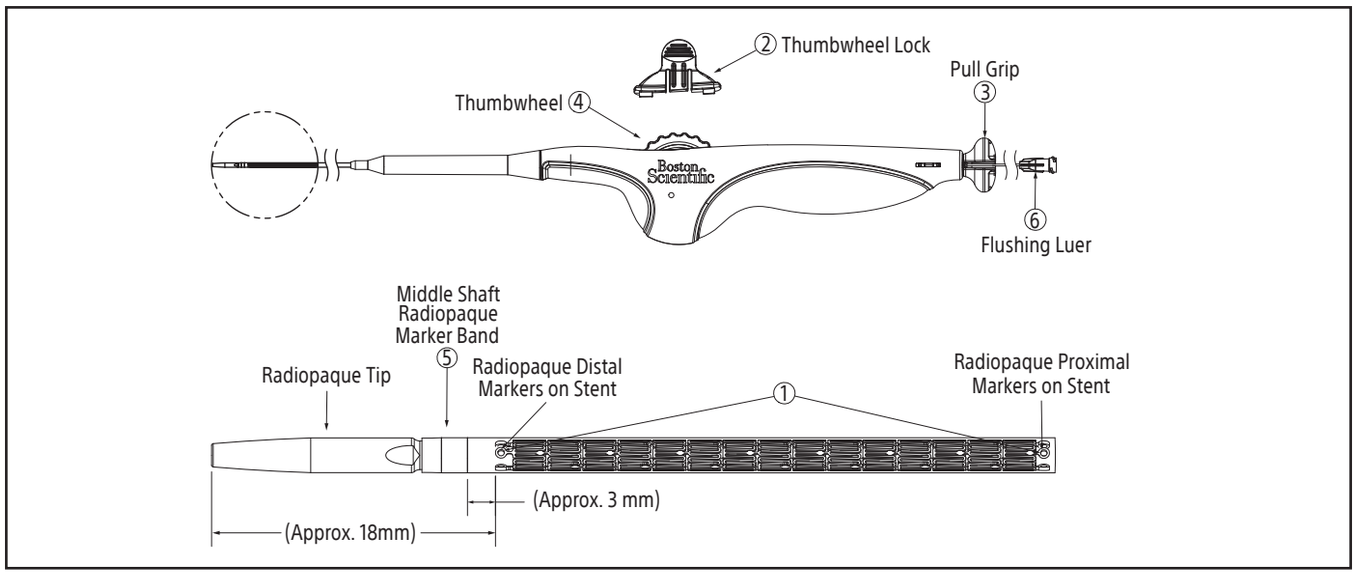

Figure 4. Stent Delivery System

Precautions:

- Always use an introducer or guide sheath for the implant procedure, to protect the access site and prevent system system damage.
- Do not use a kinked delivery system. Kinking of the introducer/guide sheath at the access site can restrict the movement of the delivery system during deployment.

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2. Pass an 0.035 in (0.89 mm) guidewire of appropriate length (300 cm length recommended for 130 cm stent delivery length systems) across the target lesion or obstruction.

Notes:

- A **stiff** 0.035 in guidewire is strongly recommended for deployment of the stent, especially for tortuous anatomy and contralateral approaches. Use of undersized guidewires may lead to insufficient support of the device which can compromise stent delivery.
- If using a hydrophilic guidewire, ensure that it is hydrated at all times.

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3. Pre-dilate the lesion with a balloon dilatation catheter using conventional technique. After the lesion has been properly dilated, remove the dilatation catheter, leaving the guidewire with the tip distal to the lesion for stent system advancement.

Precaution: Physicians should use judgment based on experience in dilating arterial lesions and/or obstructions. Never force a balloon catheter to inflate to the point of risking dissection of the arterial wall.

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4. Place the ELUVIA Drug-Eluting Vascular Stent System over the guidewire. Advance the delivery system as a unit through the hemostatic valve of the introducer or guide sheath.

Notes:

- Do not tighten Tuohy-Borst such that it restricts the movement of the delivery system.
- Do not remove the thumbwheel lock prior to deployment. Premature removal of the thumbwheel lock may result in an unintended deployment of the stent.

10.9 Stent Deployment Procedure

1. Remove slack from the system by advancing the system just beyond the target lesion, then, pulling the system back until stent radiopaque markers ① are centered over the target lesion.

Note: Prior to deployment, ensure adequate distance between the proximal end of the stent and the introducer/guide sheath to prevent deployment within the introducer/guide sheath.

2. Remove the thumbwheel lock ② by compressing the tabs and pulling. Confirm that the radiopaque markers are still properly positioned across the target lesion.

Precaution: If strong resistance is met with the introduction of the delivery system or if unable to initiate release of the stent, remove the entire system from the patient and introduce a new system.

Notes:

- For optimal performance, keep the entire length of the delivery system that is outside the body as straight and stable as possible. To do so, remove slack from the system, maintain slight backward tension on the delivery system, and anchor the handle on the patient or operating table during deployment. Alternatively, the operator may straighten and stabilize the distal end of the blue outer shaft during deployment.
- Failure to eliminate slack (Reference **Figure 5**) and/or curvature of the delivery system catheter between the introducer/guide sheath and the delivery system handle during deployment may adversely affect deployment accuracy, especially in ipsilateral cases.
- If repositioning of the stent delivery system is required, reinserting the thumbwheel lock will prevent inadvertent deployment.

Figure 5. Eliminate Slack

10.10 Recommended Method of Deployment

1. While using fluoroscopy maintain position of the distal and proximal stent radiopaque markers ① relative to the targeted site. Roll the thumbwheel ④ of the deployment handle in the direction of the arrow indicated on the handle. Continue to roll thumbwheel until the middle shaft radiopaque marker band ⑤ passes the distal stent radiopaque markers. Watch for the distal stent radiopaque markers to begin separating: separation of the distal stent radiopaque markers signals that the stent is deploying.
2. Continue to roll thumbwheel until the middle shaft radiopaque marker band ⑤ passes the proximal radiopaque markers of the stent resulting in full deployment, or until the white activation arrow is visible on pull grip extension rod (for 150 mm length stents), which indicates that pull grip activation is required to complete stent deployment (Reference **Figure 6**). Long stents (150 mm) will not be fully deployed by the thumbwheel alone.

Notes:

- When activating the pull grip, avoid rapid deployment.
- Do not restrict movement of the thumbwheel ④ otherwise deployment difficulties could be encountered. Do not attempt to pull a partially expanded stent back into introducer / guide sheath as dislodgement may occur.
- Do not push or pull the delivery system during deployment as this may compromise stent length.

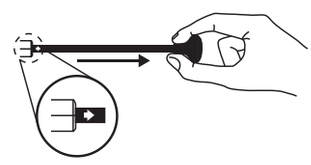

Figure 6. Long stents (150 mm) require the pull grip to be retracted only after the white activation arrow is visible to complete deployment.

3. Grasp the manual pull grip ③ and gently pull away from the handle in the direction of the arrow. Slowly pull back until the middle shaft radiopaque marker band ⑤ passes the proximal radiopaque markers of the stent resulting in full deployment.
4. View the delivery system under fluoroscopy, ensuring that the middle shaft radiopaque marker band ⑤ has crossed the proximal stent markers. The delivery system can now be withdrawn.
5. Grasp the guidewire a short distance from handle and repeatedly retract the system over the wire until fully removed. Use caution when withdrawing the stent delivery system and always manipulate under fluoroscopy. If unusual resistance is felt, carefully readvance and rotate the delivery system in an attempt to center the delivery system within the vessel, then carefully attempt to repeat withdrawal.

Note: Avoid bending the guidewire excessively near handle when retracting device to aid removal and prevent guidewire kinking, especially when using guidewires with diameters smaller than recommended.

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6. If incomplete expansion exists within the stent at any point along the lesion, balloon dilatation can be performed utilizing standard PTA technique.

Precaution: Never pre-dilate the stent using a balloon that is larger in diameter than the nominal (labeled) diameter of the stent.

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7. Withdraw guidewire and sheath from patient and establish hemostasis per conventional technique.

10.11 Disposal

To minimize the risk of infection or microbial hazards after use, dispose device and packaging as follows:

After use, device and packaging may contain biohazardous substances. Any device and packaging that came into contact with biohazardous substances should be treated and disposed of as biohazardous waste or be treated and disposed of in accordance with any applicable hospital, administrative, and/or local government regulations. Use of a biohazardous container with biological hazard symbol is recommended. Untreated biohazardous waste should not be disposed of in the municipal waste system.

10.12 Post Procedure

Assess patient for hematoma and/or other signs of bleeding at the puncture site.

11. REFERENCES

The physician should consult recent literature on current medical practice on stent implantation.

12. WARRANTY

Boston Scientific Corporation (BSC) warrants that reasonable care has been used in the design and manufacture of this instrument. **This warranty is in lieu of and excludes all other warranties not expressly set forth herein, whether express or implied by operation of law or otherwise, including, but not limited to, any implied warranties of merchantability or fitness for a particular purpose.** Handling, storage, cleaning and sterilization of this instrument as well as other factors relating to the patient, diagnosis, treatment, surgical procedures and other matters beyond BSC's control directly affect the instrument and the results obtained from its use. BSC's obligation under this warranty is limited to the repair or replacement of this instrument and BSC shall not be liable for any incidental or consequential loss, damage or expense directly or indirectly arising from the use of this instrument. BSC neither assumes, nor authorizes any other person to assume for it, any other or additional liability or responsibility in connection with this instrument. BSC assumes no liability with respect to instruments reused, reprocessed or resterilized and makes no warranties, express or implied, including but not limited to merchantability or fitness for a particular purpose, with respect to such instruments.

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